The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 113, No. 7 — COPYRIGHT, 1939, BY AMERICAN MEDICAL ASSOCIATION CHICAGO, ILLINOIS — AUGUST 12, 1939

CHRONIC INTRACTABLE ULCERATIVE COLITIS—A SURGICAL PROBLEM

CHAIRMAN'S ADDRESS

HENRY W. CAVE, M.D.

NEW YORK

Failure of conservative, or medical, measures is leading to surgical intervention in an increasing number of cases of chronic ulcerative colitis. Clinicians who have had extensive experience with the disease are at present prone to be cautious in accepting the term "cure." Many forms of treatment have been recommended—rest in bed, high caloric, high vitamin, low residue diets, vaccines, serums of various types, including antistreptococcus, anticolon bacillus and antidysentery, sulfanilamide and other chemical agents, blood transfusions and medicated irrigations. Not infrequently, certain of these measures are followed by temporary improvement. Less often is the improvement sustained. Usually the cycle of the disease continues and progressing pathologic change thwarts the efforts of the physician and destroys the health and usefulness of the patient. "It is impossible to say that after any given period of freedom from activity the disease will not recur."[1] Certainly in the past many patients have been lost because radical surgical measures were denied them.

It may be stated generally, however, that surgical intervention should be delayed until two factors have been evaluated: (1) the response to conservative treatment and (2) the extent and distribution of permanent damage to the colon.

During the past three years my associates and I have had an unusual opportunity to study intensively many cases of ulcerative colitis. A specially equipped laboratory and a clinical service have been established for investigating the mechanism of this and allied diseases. Two hundred and fifty-seven patients have been carefully studied, classified and followed by Dr. Thomas T. Mackie and his medical associates, some for as long as seven years; 158 of these have been treated in the Gray service of the Roosevelt Hospital. Twenty-seven of the latter group have been subjected to surgical intervention. It is from this experience that the title of this paper has been derived. We have as well ascertained certain facts and have formulated conclusions which appear worthy of presentation.

An attempt has been made to divide, although somewhat empirically, these patients into four classes: (1) those with a mild form, arrested and perhaps cured by medical management alone (this class is excluded from the discussion); (2) those with the acute fulminating, often fatal form; (3) those with the chronic continuous form, and (4) those with the chronic form with remissions, which is frequently intractable.

There is little unanimity of opinion concerning the indications for elective operation. There are few criteria for determining operability. These two fundamental problems at times are difficult of solution, yet they must be solved if successful results are to be achieved. The former depends on the local pathologic change, the latter on the general condition of the patient as well as on the pathologic change.

The disease is characterized by inflammation and ulceration of the colon, cellular infiltration and marked production of scar tissue. This process commonly extends with each exacerbation and recurrence of the disease, producing progressive permanent damage and dysfunction, until ultimately the colon becomes transformed into a narrowed and shortened fibrotic organ lined with infected granulation tissue. When this stage has been reached, the term intractable may be applied. The effort to restore the patient to health then becomes a definite problem of elective surgical intervention.

The choice of operative procedures must be based on the extent and situation of permanent damage to the colon. These can be determined with considerable accuracy by the combination of proctoscopic examination and careful x-ray examination. The roentgenograms reveal the characteristic shortening, narrowing of the lumen, absence of haustral markings, mucosal destruction and pseudopolypoid degeneration. When the entire organ is involved, the normal angulations at the flexures tend to approximate right angles. The barium sulfate enema demonstrates a rapidly filling colon, with hyperirritability of the segments that are involved.

Perforation, impending or actual, multiple cutaneous infections and the frequently occurring and recurring perirectal abscesses naturally require immediate operation. In view of recent disastrous experiences with four fatal cases of the acute fulminating form, it seems probable that complete diversion of the fecal stream should be carried out much earlier than is usually done.

Criteria of operability are difficult to define in many conditions. They are particularly so in chronic ulcerative colitis, a disease commonly complicated by profound physiologic disturbances, including change in the plasma protein and electrolyte concentrations, inanition and marasmic states, advanced grades of vitamin deficiencies, disturbance of fluid balance and severe and refractory anemia, all of which profoundly affect the surgical mortality.

From the Gray Service, the Roosevelt Hospital.

Read before the Section on Surgery, General and Abdominal, at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 18, 1939.

1. Mackie, T. T.: The Medical Management of Ulcerative Colitis, J. A. M. A. 111:2071 (Dec. 3) 1938.

PREOPERATIVE PREPARATION

The decision to resort to operation, therefore, does not mean that medical supervision should cease. I cannot emphasize too strongly the importance of meticulous preoperative and postoperative medical control. Preparation for operation is frequently time consuming. Blood chemistry and blood vitamin determinations are made at frequent intervals. Anorexia and its effects are combated by heavy parenteral doses of thiamin chloride and at times by continuous gavage feeding of a calibrated synthetic diet. Dosage of the other vitamins, controlled by weekly or biweekly blood vitamin assays, is pushed until the curves at least approximate normal. Supplemental mineral salts are added when

TABLE 1.—*Surgical Procedures*

	Ileostomy	Ileosigmoidostomy	Partial Colectomy with Transverse Colostomy	Partial Colectomy with Removal of Rectum	Colectomy	Colectomy with Removal of Rectum
No. of patients	19	3	3	2	8	3

Five deaths, mortality 18.5 per cent.

the content of blood electrolytes is low. The frequent finding of lesions of the mouth and tongue of the pellagra type is considered an imperative indication for the administering of nicotinic acid and of liver extract parenterally. The anemia is corrected by iron or liver extract and transfusion. In addition, abundant dextrose in saline solution given intravenously is essential. The preoperative diet should be low in residue. Daily cleansing colonic irrigations of physiologic solution of sodium chloride are given, and for two days prior to operation lead and opium pills and camphorated tincture of opium are administered in order to shrink the colon, thus simplifying the technical procedure.

ANESTHESIA

Complete relaxation is necessary during the stage when the entire colon is removed. Heretofore, avertin in amylene hydrate and cyclopropane have proved satisfactory. In view of recent catastrophes, I question whether this highly explosive gas should be used as a routine. Spinal anesthetics in the form of procaine hydrochloride, or preferably pontocaine hydrochloride and nupercaine for their prolonged continuous action, may be used with relative safety. It matters little what is used at the first stage of ileostomy. I do believe, however, that ether is contraindicated during the stage of colectomy, for usually this is a two hour session.

OPERATIVE PROCEDURES

I am unquestionably skeptical of the value of appendicostomy, cecostomy and colostomy as curative measures. For the most part, the openings made into the bowel were used primarily for the purpose of irrigating the colon in the hope that some antiseptic solution would destroy invading organisms and thus effect a cure. In view of our present knowledge of the actual pathologic condition that exists, these three procedures are discarded as theoretically unsound and as actually being completely ineffectual. Complete removal of the diseased bowel is indicated and is essential to effect a "cure." Numerous operative procedures are employed; two, three or even four stages make for safety with debilitated patients. Ileostomy is usually the first stage. Through a McBurney incision the terminal part of the ileum, if uninvolved, is divided 6 inches from the ileocecal valve; the proximal 3 inches is brought well out on the anterior abdominal wall. (The longer the segment of protruding ileum, the easier it is to manage the bag or dressing.) I decry the practice of exploring the abdomen at this stage, as well as of using a right rectus incision as a site for the ileostomy opening. To prevent loops of small bowel from adhering between the right lateral abdominal wall and the proximal segment of ileum, careful closure of this space should be done. Formerly the distal part of the divided ileum was closed in layers and dropped back. This practice has been abandoned; it is safer and more convenient for the second stage to bring the distal end out as a mucous fistula just to the left of the midline of the abdomen.

It has seemed to me that the acute fulminating, often rapidly fatal, form of short duration presents difficult problems. The desperately ill patient when first seen is not a good surgical risk, even for an ileostomy, an easily performed surgical maneuver. The clinicians, attempting to bring about a remission, often have waited too long. Even though the patient has not been sufficiently studied and rehabilitated, early diversion of the fecal stream by means of a double-barreled ileostomy might prove advantageous. If later the clinical evidence and roentgenograms indicate that the disease process has been arrested in the colon, the normal fecal flow might be resumed by crushing the spur, as has been suggested by Devine for the large intestine.

Four patients in our series had the acute form of the disease and were operated on, all having been ill for a period of not longer than three months without remissions; all died, two from massive hemorrhages, one from perforation of the sigmoid colon and one from inanition. All had an ileostomy. Ileostomy is accompanied by a high mortality usually because of the seriousness of the disease, the fact that surgical aid is solicited too late, and the rapid loss of fluids and chlorides. Ileostomy alone, with no further surgical intervention, has not infrequently resulted in prolonged freedom from symptoms. Some authorities have claimed positive cures. For example, Barney and Brust [2] reported a case in which a 19 year old youth with symptoms of rapidly fulminating colitis of short duration underwent a loop ileostomy immediately, with administration of Bargen's autogenous vaccine. Three years later, sigmoidoscopic examination revealed an apparently normal sigmoid colon and rectum; the ileostomy opening was closed. In a recent communication to me Dr. Barney wrote that this patient was robust and overweight for his size and age; there were not more than three stools a day, and there were no pain and no signs of bleeding. I have performed ileostomy nineteen times as a preliminary step for total colectomy. In our series, a woman of 29 who had had the chronic continuous type for ten years had undergone ileostomy eight years before with improvement, yet because of hay fever each summer she suffered from diarrhea with bloody stools. Her disease was not sufficiently arrested, and recently, by removal of the entire colon, which was thoroughly diseased, we feel that her chance for cure was considerably enhanced.

If it has been determined that the lower, descending part of the sigmoid colon and the rectum are free from the disease, an end to side ileosigmoidostomy to divert completely the fecal current may wisely be carried out

2. Barney, C. O., and Brust, J. C. M.: New York State J. Med. **37**:1852-1853 (Nov. 1) 1937.

as a first stage procedure, with a partial or subtotal colectomy later, but let it be emphatically understood that such a procedure is applicable in less than 10 per cent of these cases. For that condition in which the terminal part of the ileum, the cecum and the ascending colon are involved, sometimes termed colo-ileitis, ileosigmoidostomy is suitable.

When the colon and rectum are involved only on the left side and the process has become sufficiently stationary, transverse colostomy is indicated. In the past, colostomies have been performed too near the diseased segment and the results, obviously, have proved unsatisfactory. Transverse colostomy produces an easily managed fecal stoma, which should be placed at least 12 inches proximal to the involved area. In the two instances in which I resorted to transverse colostomy, the disease had been restricted to the descending colon and rectum for more than three years. If patients suffering from this disease, which starts in the rectum and gradually invades the transverse and ascending colon, could be submitted to operation sooner, colostomy, which is assuredly preferable to ileostomy, would suffice.

The complete removal of the colon and rectum should be performed in three or four stages, the fourth stage reserved for the patients who are poor risks: (1) ileostomy (already discussed), (2) subtotal colectomy and (3) proctectomy.

We have performed subtotal colectomy eleven times, with one death. I draw attention to this fatality, for the patient, a boy aged 18, had presented a most unusual picture of the chronic continuous type of the disease for two years. A barium sulfate enema revealed that there existed an internal fistulous opening between the cecum, loops of terminal ileum and sigmoid colon. At operation, in an attempt to divide and close the fistulous tracts, leakage occurred. The patient died of peritonitis three days later. A long left paramedian incision affords ample exposure for removal of the entire colon and

TABLE 2.—*Mortality Rates for Ulcerative Colitis*

Total patients	257	
Gross mortality	25	9.7%
Medical deaths	16	6.2%
Surgical deaths	9	22.5%
Total patients operated on	40	
Patients treated at Roosevelt Hospital	158	
Gross mortality	11	7.0%
Medical deaths	6	3.7%
Surgical deaths	5	18.5%
Total patients operated on	27	
Patients not included in Roosevelt Hospital group	99	
Gross mortality	14	14.1%
Medical deaths	10	10.1%
Surgical deaths	4	30.8%
Total patients operated on	13	

makes easier the division of the splenophrenocolic ligament. The omentum is detached from the transverse colon and pushed upward under the costal margins; this step simplifies the removal of the transverse colon and thus preserves the omentum for the purpose of covering raw areas and lessening the possibility of intestinal obstruction.

The terminal part of the ileum and the ascending, transverse and descending colon are removed. Care is taken to identify and protect the third portion of the duodenum and the right ureter as one exposes the retroperitoneal surface of the ascending colon and mobilizes the hepatic flexure. Immediately after the ligation of the middle colic artery as the transverse colon is being freed, there is frequently a sudden fall in blood pressure; should this occur, immediate transfusion is advisable. Because of the extensive incision and the handling of the colon, heat is lost and a certain amount of so-called shock ensues if care is not taken to keep the intestine, particularly the small intestine, cov-

TABLE 3.—*Analysis of Operative Deaths*

Sex	Age	Form of Disease	Duration of Disease	Operation	Cause of Death
♂	26	Chronic with remissions	6 years	Ileostomy	5 days postoperative; technical error; gangrene of exteriorized loop; lobar pneumonia
♂	20	Acute fulminating	3 weeks	Ileostomy	9 days postoperative; massive hemorrhage
♂	56	Acute fulminating	7 weeks	Ileostomy	6 days postoperative; massive hemorrhage
♀	32	Chronic with remissions	3 years 6 months	Ileostomy	3 days postoperative; peritonitis; abundant cloudy fluid at time of ileostomy; desperately ill
♂	18	Chronic continuous	2 years	Subtotal colectomy	3 days postoperative; peritonitis due to soiling following division of internal fistulous tracts

ered with moist warm gauze pads. Hemostasis is meticulously attended to so that hematomas will not form between the leaves of the cut mesentery.

By far the most technically difficult part of this entire procedure is the division of the splenophrenocolic ligament, and it is through the long paramedian incision on the left side that this ligament is most easily identified and severed.

Thus far I have had but little difficulty in dividing the lower part of the sigmoid colon over a rubber guarded clamp as advised by Rankin or in turning the stump in with several layers of interrupted silk sutures. Should there be any question of a tight closure of the stump, it is advisable to bring it out as a mucous fistula, as is done in a first stage Lahey operation for cancer of the rectum.

Peritonealization of the raw surface where the colon has been removed we have thus far practiced. Cattell expressed the opinion that this is unnecessary. It does not prolong the operation to any appreciable extent and does minimize the opportunity for the formation of adhesions.

After subtotal colectomy the majority of the patients improve markedly, in fact to such an extent that the question naturally arises whether and when the rectum should be removed. In four instances we have been reluctant to resect the rectum because of a tremendous gain in weight and an apparently lessened activity in the remaining segment. When a bloody discharge continues to be extruded from the anal opening and there persists inflammatory involvement in the perirectal space, with or without the presence of fistulous openings, it seems preferable to perform proctectomy.

The third stage of the radical treatment is best carried out by the combined abdominoperineal resection in one stage, after the Miles technic. We are now accustomed to close the posterior wound tightly except for a small rubber tube drain near the tip of the coccyx. This practice has diminished considerably the period of convalescence and we feel, despite some opposition, that it is a justifiable procedure.

A question often asked is how much time should intervene between the stages. From the stage of ileostomy to subtotal colectomy from three to eight months is usually allowed; from subtotal colectomy to resection of the rectum, four months seems sufficient.

Immediately after the close of each of these procedures, transfusion has unquestionably proved timely and beneficial.

Associated disorders, such as deficiency states, avitaminosis, rectovaginal and perirectal fistulas, delayed puberty, lack of skeletal growth, rickets, secondary anemia, tetany, and beriberi, have not simplified the surgical problems and added to the patients' safety; therefore every safeguard should be utilized for protection.

COMPLICATIONS

The commonest postoperative complication is peritonitis, frequently the result of perforation or soiling from technical mishaps during the process of colectomy. Persistent hemorrhage, pneumonia, sepsis, inanition, embolism, mechanical and paralytic ileus and thrombophlebitis are other hazards. The most striking feature of the surgical management of this disease is the enormous gain in weight, even after ileostomy alone

Table 4.—*Causes of Medical Deaths*

	No. of Cases
Perforation	5
Pneumonia	3
Sepsis	1
Pneumonia and paralytic ileus	1
Carcinoma, site unknown	1
Inanition	1
Embolism	1
Nephrosis	1
"Colitis"	1
Unknown	1

but more particularly after removal of the entire diseased colon. There has resulted an average gain of 42 pounds (19 Kg.) by the twenty-two patients who survived operation.

MORTALITY

Of a total of 257 patients studied, 158 were treated at the Roosevelt Hospital, with a gross mortality of 7 per cent. Six patients in this group died while under medical supervision, a mortality of 3.7 per cent. Twenty-seven patients were operated on; five of these died, giving an operative mortality of 18.5 per cent. Of the miscellaneous group (those not treated at the Roosevelt Hospital), which is presented for comparison, all have been followed by Dr. Mackie, many in the ulcerative colitis clinic, but were operated on in other institutions by other surgeons, ninety-nine in all, with a gross mortality rate of 14.1 per cent. Ten of this number died while under medical care, a mortality of 10.1 per cent. Thirteen were operated on, with a mortality rate of 30.8 per cent. This comparison is purposely drawn to emphasize the importance of a combined, carefully planned and meticulously followed approach between the physician and the surgeon who are directly in charge of the patients. These two groups, the Roosevelt Hospital group and the miscellaneous group, make a total, as has been stated, of 257 patients. The total mortality rate, i. e. medical and surgical combined, was 9.7 per cent. Sixteen died while under medical care, a mortality of 6.2 per cent. Of the forty patients operated on nine died, thus giving, for the two groups combined, a mortality rate of 22.5 per cent.

COMMENT AND CONCLUSIONS

Although twenty-seven patients operated on for this disease is not a large number, we feel that it is of sufficient size for the formulation of certain conclusions. If the condition of such desperately ill patients cannot be controlled completely by medical management, surgical intervention is essential; although they are bad risks, if the operative mortality rate is kept below 20 per cent, more patients should be given the opportunity for cure. A more detailed analysis of the five deaths among the twenty-seven patients operated on at the Roosevelt Hospital reveals that one patient, a man, desperately ill, died because of a technical error on my part. In an attempt to make ileostomy safer, I brought out on the anterior abdominal wall a loop of the terminal part of the ileum with the idea of opening it twenty-four or thirty-six hours later. Unfortunately, there was an embarrassment of the circulation with resulting gangrene and peritonitis. The second patient was a woman with a large distended abdomen filled with cloudy fluid, whose temperature was 102.5 F. and whose colon I believe had perforated before ileostomy was done. Two other patients were admitted to the hospital during an activated stage with massive hemorrhages and marked abdominal distention; ileostomy was attempted in the hope of staving off death. The fifth patient was the only one in the series to die after colectomy from peritonitis due to soiling at the time of disentanglement of internal fistulous tracts between the cecum, terminal ileum and sigmoid colon. Every effort is now being made to reduce the mortality by careful estimation of just how much surgical intervention the patient can tolerate, and I again emphasize that medical supervision should not cease at the time of operation.

Surgical intervention is indicated for perforations, repeated hemorrhages and strictures, for diffuse polyposis with or without malignant involvement and for conditions not relieved by medical management. Opinion varies concerning the indications for elective operation. As yet no definite criteria have been established for determining operability. Operative procedures must be based on and determined by the extent and situation of permanent damage to the colon. Preoperative and postoperative medical supervision is essential to the successful outcome, for the patients are dehydrated, anemic, septic and often semicadaverous. It is difficult to determine whether to intervene surgically and when to do so with patients suffering from the acute fulminating, often rapidly fatal, form of this disease.

If the colon and rectum are involved only on the left side, transverse colostomy (in the healthy part of the bowel), with removal of the colon and rectum on the left, is justified. Should the colon be diseased on the right side and the rectum and sigmoid colon not involved, ileosigmoidostomy followed by subtotal colectomy is sufficient.

With extensive disease of the entire colon, removal of the affected bowel is accomplished in three or four stages. When the stage of intractability has been reached, elective operation, in spite of a mortality of about 20 per cent, offers more than a continuation of medical treatment.

Of 158 patients admitted to the Gray service, twenty-seven were operated on and five died, an operative mortality of 18.5 per cent. An average gain in weight of 42 pounds (19 Kg.) and marked clinical improvement justify surgical intervention, not for complications alone but in order to eradicate the disease.

USE OF GUANIDINE HYDROCHLORIDE IN TREATMENT OF MYASTHENIA GRAVIS

ANN S. MINOT, PH.D.
KATHARINE DODD, M.D.
AND
SAMUEL S. RIVEN, M.D.
NASHVILLE, TENN.

We[1] have reported that the function of muscles in patients with myasthenia gravis is temporarily improved by the administration of guanidine hydrochloride. The present discussion gives a more detailed account of our experience with the use of guanidine for the treatment of this disease. Altogether we have now observed the action of the drug in seven persons with myasthenia gravis. In five instances outlined in the following case reports we have been able to observe the patients for a considerable period. One of the other two patients was a Negress with mild myasthenia gravis complicated by marked hypothyroidism. In this instance a typical response to guanidine was elicited but medication has not been continued further. The other person had had myasthenia gravis for several years but was in a state of practically complete remission following thymectomy. This woman gave the same slight response to guanidine seen in some normal persons.

REPORT OF CASES

CASE 1.—H. C., a boy aged 13 years, was admitted to the hospital July 31, 1937, with a history of weakness, fatigability and difficulty in talking and swallowing of three months' duration. He had an expressionless face, ptosis of the eyelids, a nasal voice and marked weakness of all the skeletal muscles. The ergographic records (fig. 1) show the response to 1 cc. of prostigmine solution injected hypodermically. He was given orally several doses of prostigmine daily and did well for a time. Gradually, however, he required more and more prostigmine. By the middle af October he required 15 mg. of prostigmine by mouth every hour in order to be able to swallow and breathe. In addition, frequent hypodermic injections of the drug had to be given. If medication was withheld, artificial respiration became necessary. Because the response to prostigmine seemed to be decreasing, it was decided to try the effect of guanidine. It was impossible because of his condition to withhold prostigmine medication entirely in order to try the effect of guanidine alone. However, October 17, one hour after a dose of prostigmine had been given, 20 mg. of guanidine hydrochloride per kilogram, dissolved in physiologic solution of sodium chloride, was administered intravenously. Within ten minutes there was a marked increase in strength (fig. 2). Thirty minutes after the dose was given the patient was stronger than he had been for several weeks and was able to roll himself around the ward in a wheel-chair. The improvement persisted for from four to five hours and then gradually decreased. The treatment with prostigmine was thereafter supplemented by daily doses of guanidine and much better muscle function was maintained than on prostigmine alone. Unfortunately, a few days later bronchopneumonia developed and the patient died.

The results of guanidine therapy were encouraging, but there was no opportunity to determine what continued treatment would have accomplished in this case of myasthenia gravis.

CASE 2.—M. O., a white woman aged 37, a housewife, was admitted to Vanderbilt Hospital Jan. 26, 1938, for a trial of guanidine medication.

A diagnosis of myasthenia gravis had been made in 1933. In the interval between 1933 and the present admission the patient had been treated with ephedrine, aminoacetic acid and prostigmine. Ephedrine and aminoacetic acid gave only slight relief and in January 1935 her condition became worse. At this time she experienced difficulty in eating and talking and

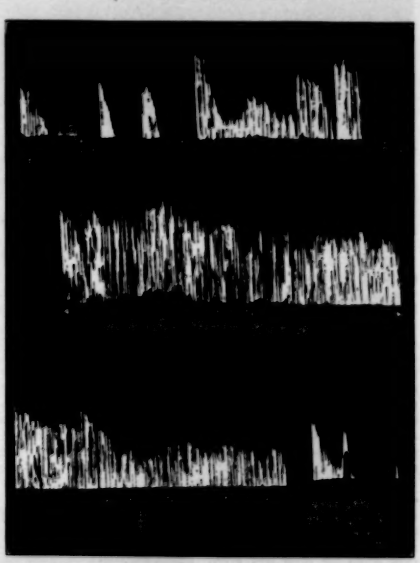

Fig. 1 (case 1).—Response to 1 cc. of prostigmine injected hypodermically.

was unable to arise from a chair without help. In April 1935 she was given a test dose of prostigmine with marked improvement in muscular power. From that time until the present admission she had taken 50 mg. of prostigmine daily in divided oral doses. On this treatment she was able to get about the house, take care of her room, dress and bathe herself and take short rides in a car. She tired quickly, however, and complained of the "let down" that came on as the effect of each dose of prostigmine wore off.

On admission in January 1938 the patient was large and well nourished. When prostigmine was withheld for a few hours she showed marked general muscular weakness. She was unable to raise herself to a sitting position in bed. Her hand grip was good at first but fatigued almost completely in twenty seconds. The face was smooth and somewhat expressionless; there was weakness of all the facial muscles and those of the jaws and neck. There was ptosis of the eyelids. Her voice was somewhat nasal, enunciation was poor and there was fatigue from continued conversation. No muscular atrophy or fibrillary twitchings were observed.

From the Departments of Pediatrics and Medicine, Vanderbilt University School of Medicine.

This work was aided by a grant from the Division of Medical Sciences of the Rockefeller Foundation.

Because of lack of space, this article is abbreviated in THE JOURNAL. The complete article appears in the authors' reprints.

Read before the Section on Nervous and Mental Diseases at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 17, 1939.

Most of the guanidine hydrochloride that we used in our experimental and clinical work was purchased from the Eastman Kodak Company in Rochester, N. Y. We obtained equally good results with guanidine hydrochloride furnished by the Calco Chemical Company in Bound Brook, N. J. The Eastman Kodak product may now be procured in tablet form for investigational purposes, according to the regulations of the Food, Drug and Cosmetics Act, from Davies, Rose & Co., Ltd., 22 Thayer Street, Boston. We are now using tablets containing 125 mg. of guanidine hydrochloride that we purchased from this company.

1. Minot, Ann S.; Dodd, Katharine, and Riven, S. S.: The Response of the Myasthenic State to Guanidine Hydrochloride, Science 87: 348 (April 15) 1938.

January 26 all drugs were withheld. Within twenty-four hours myasthenic symptoms were marked. Preliminary ergographic tracings were made (fig. 3) and 1 cc. of prostigmine solution (0.5 mg.) was injected intramuscularly. A typical marked improvement in muscle function resulted. The facial expression became less stiff and the patient could raise herself easily from bed. Within two or three hours after medication her weakness was as marked as before the injection.

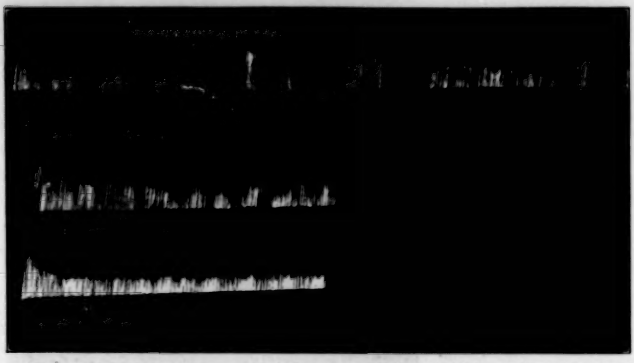

Fig. 2 (case 1).—Response to intravenous injection of guanidine hydrochloride one hour after dose of prostigmine.

No further prostigmine was given. January 29, 10 mg. of guanidine hydrochloride per kilogram dissolved in physiologic solution of sodium chloride was injected intravenously. Within ten minutes the patient remarked on her feeling of increased strength, and ergographic tests indicated marked improvement. No undesirable symptoms were produced by this dose. The only sensation other than improved strength noted by the patient was a tingling of the lips and finger tips for a few minutes after the injection. Control injections of physiologic solution of sodium chloride gave entirely negative results. January 31 a slightly smaller dose of 6.6 mg. of guanidine hydrochloride per kilogram was given intravenously. There was the same prompt improvement in muscular strength, which had not entirely disappeared after eight hours (fig. 4). Again no undesirable symptoms were noted. February 2 the same dose of guanidine hydrochloride (6.6 mg. per kilogram) was administered by mouth. The response was only slightly slower than when the drug was given by vein. The same tingling sensation was noted and within thirty minutes there was a marked improvement in strength, which persisted about seven hours.

The problem from this point on was to adjust the doses of guanidine and the time of administration to get as well sustained and as even a level of improved function as possible. We now know that our progress in getting this patient on adequate treatment was unnecessarily slow. At the time, however, we were much more familiar with the intoxication produced by guanidine (discussed later in this paper) than with its therapeutic use and deemed it wiser to proceed carefully, with frequent chemical studies of blood and urine and measurements of blood pressure. The patient was kept in the hospital for a week on 10 mg. of guanidine per kilogram a day in three divided doses. The strength was fairly well maintained on this treatment. No undesirable symptoms were noted and the concentration of guanidine in the blood in spite of medication was only 0.39 mg. per hundred cubic centimeters (an entirely normal figure) on the day of discharge.

The patient was sent home on 11 mg. of guanidine hydrochloride per kilogram daily and was seen each week for general check-up and chemical studies. On each visit the patient reported no undesirable symptoms and asked to have the drug increased. By March 1 the daily dose was 20 mg. per kilogram and the patient was feeling considerably better than when on prostigmine. A sample of blood taken about two hours after the morning dose of guanidine showed only 0.41 mg. per hundred cubic centimeters. The blood pressure was 125 systolic, 88 diastolic. In April the dose was increased to 22 mg. per kilogram a day and in May to 28 mg. This total daily dose has been continued until the present time. On this treatment the patient is able to take complete care of herself and her room and do light work about the house. She enjoys picnics, rides and visits to her friends without extreme fatigue. Her knees still tire after a short walk but regain their strength after a short period of rest. There is no evidence of facial weakness at any time and no periods of complete "let down." No atropine has been administered. Only an occasional single tablet of prostigmine has been taken before some especially strenuous activity. The highest level of guanidine in the blood noted at any time was 0.48 mg. per hundred cubic centimeters on one occasion two hours after she had taken a dose of 15 mg. per kilogram of the drug.

From the progressive gradual increase in dosage of guanidine in this case from the beginning of treatment to the present time one might conclude that tolerance was being acquired and that more and more of the drug was required. This was really not the case. The dose was not increased because a given amount of the drug had become less effective than previously but because we learned with further experience that larger amounts could be given with safety and with additional improvement in muscular function.

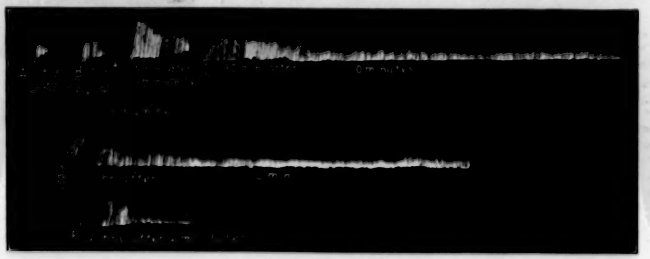

Fig. 3 (case 2).—Response to 1 cc. of prostigmine given hypodermically.

Evidence that this patient is being maintained by guanidine and is not in a spontaneous remission is offered by the fact that on one occasion medication was withheld for a day. Her weakness returned and she collapsed in walking across the room and was unable

to rise from the floor without aid. As soon as a dose of guanidine was administered her strength promptly improved.

CASE 3.—H. W. C., a white woman aged 47, represents another case of myasthenia gravis of long standing. She came to Vanderbilt Hospital for observation and a trial of guanidine therapy.

On admission the patient was pale, fairly well developed and nourished and mentally alert and cooperative. Without medication there was marked generalized muscular weakness with rapid fatigue on repeated effort. The facial expression appeared stiff and "frozen." There was slight ptosis of the eyelids. Ocular movements were restricted and poorly sustained in all directions and convergence was poor. Enunciation was poor and the voice became almost inaudible after five minutes of speaking at a conversational pitch. The deep reflexes were physiologic but were soon exhausted by repeated stimulation.

On May 3 all medication was discontinued. May 5, 1 cc. of prostigmine solution was given intramuscularly. Within fifteen minutes the patient's voice was stronger, enunciation was more distinct and a marked improvement was observed in the muscles of the face and limbs. Ergographic records were obtained which gave further evidence of increased strength. Within two hours, however, the effect of medication was rapidly wearing off and somewhat later there was a period of depression during which the patient appeared weaker than before prostigmine was given.

Prostigmine was then discontinued entirely. May 6, 10 mg. of guanidine hydrochloride per kilogram was administered orally. Within thirty minutes there was marked improvement in muscular strength, which the ergographic records show persisted in a gradually decreasing degree for five hours (fig. 5).

Profiting by our experience in the previous case, we increased the administration of guanidine much more rapidly in this case, as shown in the accompanying table.

This amount of guanidine caused no undesirable symptoms, and muscular strength was maintained throughout the day at about the level attained shortly after a dose of prostigmine.

Since her return home she has continued to take daily from 25 to 30 mg. of guanidine hydrochloride per kilogram by mouth. She writes that she can take automobile rides and short walks without exhaustion. This summer she spent a week at the seashore during which time she enjoyed picnics, bathing (not swimming) in the ocean, sketching, painting and reading. She finds it necessary to lie down to rest only about an hour a day. Her eyes are normal (with glasses) and her voice and facial expression have become normal. Before the development of myasthenia gravis she had been a commercial artist. Now for the first time in several years she has been able to resume this type of work at home for a few hours a day without marked fatigue. Occasionally she takes one tablet of prostigmine before unusually strenuous activity. There have been no undesirable symptoms other than tingling of the fingers after a dose of guanidine and an occasional bad taste in the mouth from regurgitation of the drug.

CASE 5.—W. M. G., a white unmarried woman aged 32, admitted to Vanderbilt Hospital Aug. 1, 1938, complained chiefly of weakness.

On admission the patient was slender and poorly developed with marked generalized weakness. Except for a short time after a dose of prostigmine she was unable to move herself in bed or to make more than the feeblest attempts to move her hands and arms. She could not speak above a whisper, and enunciation was indistinct. Her eyelids drooped and she could not raise them; her facial muscles moved only slightly, and difficulty in swallowing caused the saliva to run from her mouth. There was rather marked deafness, especially on the left. Bone conduction was normal. She had a small external hemorrhoid. No cause was found for the slight tenderness and occasional pain in the right lower quadrant. The remainder of the physical examination was essentially negative. The reflexes were present but somewhat hypo-active. The blood pressure was 110 systolic, 80 diastolic. The daily creatinine output in the urine was approximately 0.7 Gm. with occasional small amounts of creatine. The hemoglobin content was 12.2 Gm. per hundred cubic centimeters; the white blood cell count was 4,700. Nonprotein nitrogen was 34 mg. per hundred cubic centimeters. The Wassermann reaction was negative. Roentgenograms showed no evidence of thymic tumor.

Because of her inability to chew and swallow, the patient was considerably dehydrated and emaciated and weighed only 86 pounds (39 Kg.). After brief observation it was apparent that before any medication could be evaluated her fluid balance must be restored and her state of nutrition improved. The management of this case was therefore necessarily rather different from those previously studied. It was obviously impracticable at first to withhold prostigmine medication in order to study the patient's response to and tolerance for guanidine alone. During the first part of her stay in the hospital prostigmine medication

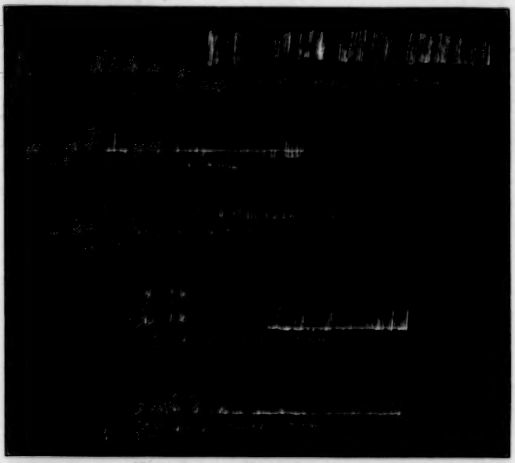

Fig. 4 (case 2).—Response to 6.6 mg. of guanidine hydrochloride per kilogram injected intravenously.

was continued, the drug being given orally when possible and hypodermically when necessary because of her inability to swallow. Guanidine, in varying doses ranging from 10 to 35 mg. per kilogram a day, was given as a supplement to prostigmine. On this regimen the patient showed considerable general improvement. She could eat and drink without difficulty and was able to be up in a chair. She gained 6 pounds (2.7 Kg.).

Increase of Dosage of Guanidine Hydrochloride in Case 3

	Dose, Mg. per Kg.	Number of Divided Doses
May 7	15	3
May 9	20	4
May 10	25	4
May 11	30	4

September 5, more extensive studies for the evaluation of different types of medication were undertaken. Since the patient became so helpless without any medication, it seemed safer and more practicable to estimate the effectiveness of guanidine by using it as a supplement to a given constant level of prostigmine medication rather than to attempt to use guanidine alone. Accordingly, guanidine medication was withheld and the patient was given eight oral doses of 15 mg. of prostigmine daily.

This amount was chosen because previous experience had shown that it was just about the limit of her tolerance for prostigmine without the production of intestinal symptoms. On this medication alone the patient was considerably weaker than she had been on the previous combined treatments. After each dose of prostigmine there was temporary improvement in strength, but she complained of feeling nervous and of the marked "let down" as the effects of the drug wore off. She did not feel strong enough to be up in a chair. September 7, while this plan of treatment was continued, ergographic tracings were obtained at intervals of approximately three hours throughout the day (fig. 6). Strength was slight and poorly sustained at all times. September 8 the amount and time of administration of the doses of prostigmine were kept the same, but four oral doses of 250 mg. each of guanidine hydrochloride were given, one dose before each meal and one at 9 p. m. This total amount of guanidine represented a daily intake of approximately 25 mg. per kilogram. On this medication the patient felt stronger and wanted to get up in a chair, but in order to make a fair comparison of objective tests she was kept in bed. Ergographic tracings were again made at the same times as on the preceding day (fig. 7). Considerable improvement can be seen in each test as compared to the records obtained on prostigmine alone. There were, however, still periods in the day when strength was poorly sustained. The amount of guanidine was then increased to six and later to seven doses a day. The patient was allowed to be up in a chair and about the ward. No untoward symptoms developed and the guanidine levels of the blood determined on various occasions were always within normal limits. This treatment was continued for several days with some rearrangement of the divided doses in an attempt to eliminate periods of weakness.

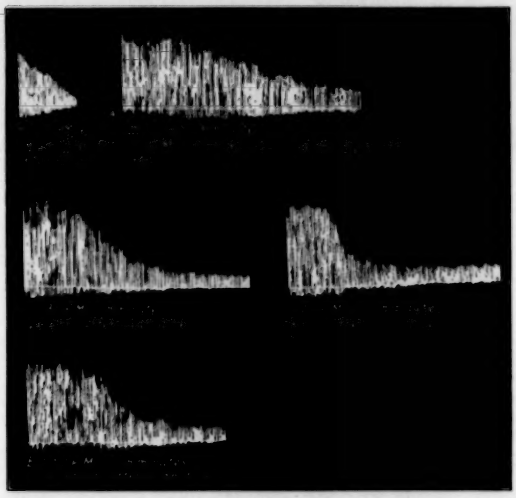

Fig. 5 (case 3).—Response to 10 mg. of guanidine hydrochloride per kilogram by mouth.

During this time the patient was closely observed and frequent ergographic tests were carried out which cannot all be presented here. Although the improvement after the addition of guanidine was quite marked, we were not satisfied with the response in this case as compared to that elicitated in cases 2 and 3. It appeared as if something were lacking in this patient which neither guanidine nor prostigmine could restore to the extent possible in some other patients. In spite of increasing the prostigmine to ten doses a day and continuing seven doses of guanidine, there was still a period of rather marked weakness in the late afternoon. Since the hyperirritability produced in normal muscles by guanidine can be controlled by extra calcium,[2] it seemed possible that we might enhance the effect of guanidine on the muscular activity of this patient by giving extra potassium. Accordingly, starting September 11, 8 cc. of a 25 per cent solution of potassium citrate was given orally three times a day in addition to the drugs already in use. Apparently because of this addition, or at any rate coincident with it, the patient became considerably stronger and more active. Attendants in the ward who were not interested in the study remarked on the improvement, and the patient said that she felt better than she had for a long time. Ergographic tracings (fig. 8) taken at various times during the day and even at the usually poor hour of about 4:30 p. m. showed well sustained muscular strength. She began to walk about the ward more and could walk the length of a long hospital corridor and back with only moderate fatigue. During the last week of her stay in the hospital the administration of potassium citrate was continued and the amount of prostigmine was gradually reduced until only four doses were given. The guanidine hydrochloride was increased to eight doses of 250 mg. a day, making a total of about 45 mg. per kilogram—still without untoward symptoms and without any persistent elevation of guanidine in the blood.

September 22 the patient was discharged with directions to continue the combined medication of four doses of prostigmine, three doses of potassium citrate and eight doses of guanidine hydrochloride and to return in one month. She was seen in the outpatient clinic October 21, having come from her home, a distance of 100 miles, by bus. She reported that she had been feeling well and that she had been able to be up and about the house most of each day. She had gained 6 pounds. The blood pressure was normal. The level of guanidine in the blood was not significantly elevated in spite of the fact that the patient had already taken four doses of guanidine on the day she was seen.

COMMENT

The foregoing reports and ergographic records demonstrate that appropriate doses of guanidine hydrochloride given either alone or as a supplement to prostigmine induce a marked improvement in the functions of the muscles of persons with myasthenia gravis without the production of untoward symptoms. The drug may be administered either intravenously or orally and is about equally effective by these two routes. Solutions of guanidine hydrochloride are too irritating for subcutaneous or intramuscular use. Except in instances in which the patient is unable to swallow, the only practical method for continued use of the drug is by the oral route. We have used a 2 per cent solution in physiologic solution of sodium chloride for intravenous injection and have given the drug orally in gelatin capsules. We have found 10 mg. per kilogram a safe and adequate amount to give as a single dose to test the effectiveness of guanidine hydrochloride in a given individual. For continued medication the total daily dose, the times of administration of divided doses, the relative amounts of guanidine and prostigmine to be used must all be worked out in terms of the needs and tolerance of each individual patient. It has been our

2. Föhner, H.: Curarestudien: I. Die periphere Wirkung des Guanidins, Arch. f. exper. Path. u. Pharmakol. 58:1 (Dec. 18) 1907. Minot, Ann S., and Cutler, J. T.: Guanidine Retention and Calcium Reserve as Antagonistic Factors in Carbon Tetrachloride and Chloroform Poisoning, J. Clin. Investigation 6:369 (Dec.) 1928.

experience that a more evenly sustained level of improved function without a sensation of nervousness and without periods of sudden "let down" can be maintained on a regimen in which guanidine makes up a large part of the necessary medication. In one instance potassium citrate appeared to increase the effectiveness of prostigmine and guanidine.

Fig. 6 (case 5).—Tracings made at intervals of three hours during a day in which eight doses of prostigmine were given by mouth. At 4 p. m. the patient was too weak to attempt a test.

Much more work will have to be done before any final explanation can be offered either for the cause of the dysfunction in the myasthenic state or for the beneficial action of prostigmine and of guanidine in this condition. In our earlier paper we [1] outlined a working hypothesis which served as a basis for the therapeutic trial of guanidine in myasthenia gravis. Summarized briefly, the hypothesis rested on the following premises:

1. Acetylcholine plays an essential role in the normal transmission of nerve impulses to skeletal muscles.[2]

2. Physostigmine or the more commonly used prostigmine hinders the destruction of acetylcholine by an enzyme (choline esterase) which is normally present in the body.[4]

3. In myasthenia gravis there is some interference with the transmission of impulses across the myoneural junction.

4. An abnormality in the participation of acetylcholine in the transmission of motor impulses in myasthenia gravis is indicated by the effectiveness of prostigmine in temporarily restoring normal function in this disease.

5. There is no evidence that acetylcholine is absent or destroyed at an abnormally rapid rate in myasthenia gravis.[5]

6. In this disease, therefore, the muscles are less than normally responsive to a given concentration of acetylcholine.

7. Guanidine increases the sensitivity of normal muscles to the action of acetylcholine.[6]

Granted these premises, many of which are admittedly highly controversial, it appears inevitable that the administration of guanidine to persons with myasthenia gravis should enhance the effect of prostigmine or should by itself cause an improvement in the functions of muscles. Our therapeutic results are compatible with this working hypothesis.

Most of the work that has previously been reported on the pharmacologic action of guanidine is a study of the intoxication induced by the drug. Doses of from 150 to 200 mg. of guanidine hydrochloride per kilogram administered to experimental animals promptly cause an acute intoxication, which has been extensively studied.[7] Severe guanidine intoxication is characterized by nervous hyperirritability, fibrillary tremors and convulsive contractions of muscles, salivation, vomiting, diarrhea, hypoglycemia and circulatory disturbances. The maintenance of a moderately increased concentration of guanidine in the blood of normal animals by the repeated administration of smaller doses or by excessive guanidine of endogenous origin has also been shown to cause a less acute but nevertheless serious and typical intoxication.[8] The administration of calcium has been shown to control the nervous and convulsive symptoms and to furnish some relief of the other manifestations of intoxication.[9] Atropine, on the other hand, has been found to be more effective than calcium

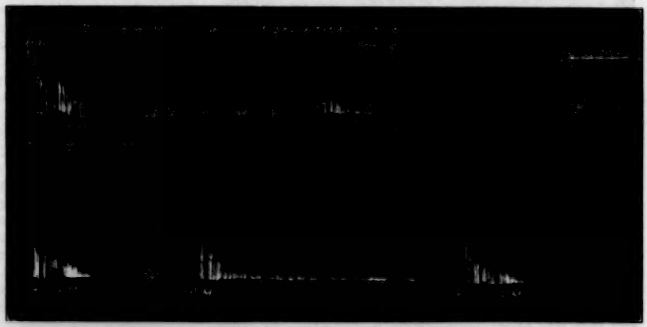

Fig. 7 (case 5).—Tracings made at intervals of three hours. Eight doses of prostigmine were given by mouth at the same time of day as on the day of tracings in figure 6 were made. In addition, four doses of 250 mg. of guanidine hydrochloride were given by mouth.

3. Dale, H. H.; Feldberg, W., and Vogt, M.: Release of Acetylcholine at Voluntary Motor Nerve Endings, J. Physiol. **86**: 353 (May 4) 1936.

4. Loewi, O., and Navratil, E.: Ueber humorale Uebertragbarkeit der Herznervenwirkung: X. Ueber das Schicksal des Vagusstoffs, Arch. f. d. ges. Physiol. **214**: 678, 1926. Loewi, O., and Navratil, E.: XI. Ueber den Mechanismus der Vaguswirkung von Physostigmin und Ergotamin, ibid. **214**: 689, 1926.

5. McGeorge, M.: Choline Esterase Activity in Disease with Special Reference to Myasthenia Gravis, Lancet **1**: 69 (Jan. 9) 1937. Milhorat, A. T.: The Choline Esterase Activity of the Blood Serum in Disease, J. Clin. Investigation **17**: 649 (Sept.) 1938.

6. Frank, E.; Nothmann, M., and Guttmann, E.: Ueber die tonische Kontraktion des quergestreiften Säugetiermuskels nach Ausschaltung des motorischen Nerven: IV. Die Wirkung der Guanidine, Arch. f. d. ges. Physiol. **201**: 569, 1923.

7. Frank, E.; Stern, R., and Nothmann, M.: Die Guanidin- und Dimethyl Guanidin- Toxikose des Säugetiers und ihre physio-pathologische Bedeutung, Ztschr. f. d. ges. exper. Med. **24**: 341, 1921. Minot, Ann S.: The Mechanism of the Hypoglycemia Produced by Guanidine and Carbon Tetrachloride and Its Relief by Calcium Medication, J. Pharmacol. & Exper. Therap. **43**: 295 (Oct.) 1931. Minot, Ann S., and Keller, Margaret: The Circulatory Failure Associated with Guanidine Intoxication, ibid. **60**: 32 (May) 1937. Minot and Cutler.[9]

8. Dodd, Katharine, and Minot, Ann S.: Incidental Hyperguanidinemia as a Cause of Clinical Tetany, Am. J. Dis. Child. **47**: 958 (May) 1934. Minot and Cutler.[9] Minot and Dodd.[10]

9. Minot and Cutler.[9] Minot and Dodd.[10] Dodd and Minot.[8] Minot.[10]

in relieving the gastrointestinal symptoms, the circulatory disturbances and the changes in blood sugar induced by guanidine but to leave the nervous and muscular changes unaffected.[10]

In view of so much emphasis on the toxic potentialities of guanidine, its use as a therapeutic agent was naturally undertaken with considerable caution. From experiments with normal dogs we found that the daily administration of from 25 to 50 mg. of guanidine hydrochloride per kilogram for several days usually caused a moderate increase in the level of guanidine in the blood, accompanied by anorexia, occasional vomiting and hyperirritability. Similarly, when normal persons took daily doses of from 15 to 20 mg. per kilogram for two or three days they complained of nervousness, increased peristalsis and, in some instances, diarrhea. Chemical studies of blood showed that these symptoms appeared when the level of guanidine was maintained

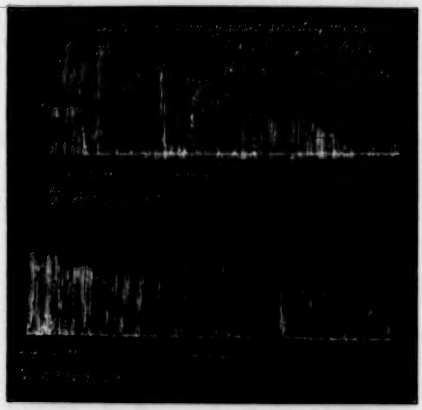

Fig. 8 (case 3).—Typical tracings obtained at intervals during a day on combined medication with prostigmine, guanidine and potassium citrate. Note the well sustained strength at usually "poor time" in late afternoon.

at from 0.5 to 0.6 mg. per hundred cubic centimeters, as compared to the normal level of from 0.35 to 0.45 mg.

When we started to treat persons with myasthenia gravis with guanidine we expected that daily doses of from 15 to 20 mg. per kilogram would increase the level of guanidine in the blood as they do in normal persons and that this hyperguanidinemia would probably cause undesirable symptoms. However, knowing that these symptoms could be controlled by atropine, we felt justified in testing the effect of guanidine on the function of muscles in patients with myasthenia gravis. As already stated in our case reports, we found that persons with myasthenia gravis can take considerably larger amounts of guanidine continuously over a long period of time than normal persons without causing any appreciable increase in the level of guanidine in the blood. A marked improvement in the function of muscles in this disease results without the production of persistent hyperguanidinemia and without symptoms of intoxication.

We do not yet know the reason for the greater tolerance of patients with myasthenia gravis to guanidine. From the prolonged effect on the function of muscles, it does not appear to be due to a more rapid excretion of the drug. It seems rather that guanidine is more readily stored or transformed into some other compound by persons with this disease. The work of Wishart [11] suggests that at least part of ingested guanidine may be transformed to creatine in the muscles. However, until more experimental work is done it is useless to speculate in regard to the mechanism involved.

There is no evidence that guanidine is of value in any of the myopathies other than myasthenia gravis. There was no immediate improvement in function in a case of pseudohypertrophic muscular dystrophy or in several persons with vague complaints of muscular weakness to whom we have given test doses of guanidine. In ergographic studies made on normal persons before and after the administration of guanidine there is occasionally evidence of slightly better sustained muscle power after the drug is taken. This does not always occur, and in any case the effect is slight. It is difficult to say whether the difference is due entirely to psychic causes or whether the slight feeling of stimulation and nervousness which guanidine causes in some normal persons causes them unconsciously to make a greater exertion.

The best guide as to the level of continued guanidine intake that is safe for a given patient is afforded by determinations of guanidine in the blood. In our experience undesirable symptoms usually accompany any persistent significant hyperguanidinemia. Samples of blood for such studies should be drawn several hours after a dose of guanidine has been taken, as there can hardly fail to be a transient increase in the blood during the rapid absorption of a dose. The determination of guanidine in the blood is a rather complicated procedure and requires laboratory facilities and some chemical experience. We use the procedure described by Minot and Dodd.[12] The results obtained by different individuals with this colorimetric method are subject to enough variation so that it is important for each person to establish his own range of values for normal blood for comparison with figures obtained after treatment with guanidine has started. The absolute values obtained are of less importance than the degree of increase as compared to normal. In practice, however, the appearance of mild gastrointestinal symptoms (loss of appetite, nausea, increased peristalsis or diarrhea) serves nearly as well as chemical studies as an early warning that the tolerance is being exceeded and that medication should be reduced or temporarily withheld.

SUMMARY AND CONCLUSION

1. Treatment with guanidine hydrochloride has caused a marked and well sustained improvement in muscular function in five cases of myasthenia gravis without the presence of undesirable symptoms.

2. Compared to normal persons, patients with myasthenia gravis can tolerate larger doses of guanidine continued for an indefinite period without the production of hyperguanidinemia.

3. Gastrointestinal and other undesirable symptoms usually appear in both normal persons and those with myasthenia gravis when any significant elevation of guanidine is persistently maintained in the blood.

10. Minot, Ann S.: A Comparison of the Effect of Calcium and of Atropine and Scopolamine on Plasma Loss and on General Symptoms of Guanidine Intoxication, J. Pharmacol. & Exper. Therap. **65**: 243 (March) 1939.

11. Wishart, G. M.: The Effect of the Injection of Guanidine on the Creatin Content of Muscle, J. Physiol. **53**: 440 (May 18) 1920.

12. Minot, Ann S., and Dodd, Katharine: Guanidine Intoxication, a Complicating Factor in Certain Clinical Conditions in Children, Am. J. Dis. Child. **40**: 522 (Sept.) 1933.

V 19

4. While these symptoms can be relieved by atropine, they should serve as a warning that the administration of guanidine should be temporarily reduced or withheld.

5. Treatment with guanidine may be combined with medication with prostigmine. In our experience, however, a more evenly sustained improvement in muscular function has been obtained when guanidine makes up a large part of the necessary medication.

6. In one case the administration of potassium citrate appeared to increase the effectiveness of treatment with guanidine and prostigmine.

7. More work is necessary before any adequate explanation can be given of the effectiveness of guanidine in restoring function to muscles in myasthenia gravis.

THE DIAGNOSIS AND TREATMENT OF MYASTHENIA GRAVIS

WITH SPECIAL REFERENCE TO THE USE OF PROSTIGMINE

HENRY R. VIETS, M.D.
AND
ROBERT S. SCHWAB, M.D.
BOSTON

The syndrome of myasthenia gravis was first suggested by Thomas Willis [1] in 1672, but the disease was not clearly delineated until the reports of Erb [2] in 1878, Goldflam [3] in 1893 and Jolly [4] in 1895. The first patient to enter the wards of the Massachusetts General Hospital with myasthenia gravis was admitted in 1905. In the period between 1905 and 1934 inclusive thirty-one patients received this diagnosis in the wards (fig. 1) and possibly a few more in the outpatient department. The disease was thus rare, only one patient a year, on the average, being seen in a moderately large general hospital. Seven of the thirty-one are known to have died either within a few weeks in the hospital or within a year at home. The disease was rapidly fatal, probably even more so since our follow-up records were not complete, than our ratio of 7 in 31 would indicate. The average age at death in this early series was slightly over 35 years. During this period, moreover, treatment was nearly unavailing. After 1930, ephedrine sulfate and aminoacetic acid were used by us with moderate success, in accordance with the experiences of Edgeworth [5] and of Boothby.[6]

A new era in the history of myasthenia gravis was begun by Walker,[7] who treated her patients with physostigmine and later with prostigmine. Her work was soon confirmed by Pritchard [8] and by Pritchard and Walker.[9] The rapid response to prostigmine given by injection led to its use as a diagnostic measure by Viets and Schwab.[10]. Harvey and Whitehill [11] and Gammon and Scheie.[12]

The oral administration of prostigmine, first proposed by Everts,[13] was extensively elaborated by Viets, Mitchell, and Schwab [14] in 1937.

Our knowledge both of the disease and of its response to prostigmine has greatly increased in the last three years, as indicated by the reports of Boothby [15] and of Kennedy and Moersch.[16]

EXPERIENCES AT THE MASSACHUSETTS GENERAL HOSPITAL FROM 1905 TO 1939

Seventy cases of myasthenia gravis have been observed between 1905 and 1939. Since treatment with prostigmine was begun in 1935,[10a] the myasthenia gravis clinic has rapidly expanded, forty-four cases being studied in the five year period from 1935 to 1939 (fig. 1). The highest incidence occurs in the second and in the fifth decade of life, but the incidence is fairly steady between the ages of 10 and 70 (fig. 2). The preponderance of patients in the early years of life,[16] usually stressed in previous reviews of the disease, has not been shown by our figures. In general the patients have shown a similar set of symptoms throughout the years. The presenting symptom in twenty-nine of seventy cases was ptosis; general weakness, dysphagia and diplopia were found in eleven, eleven and eight cases, respectively (fig. 3).

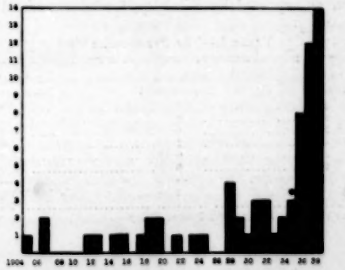

Fig. 1.—Incidence of myasthenia gravis at the Massachusetts General Hospital from 1905 to 1939; total number of cases, seventy. The asterisk indicates the introduction of prostigmine.

The prostigmine used was furnished partly by Hoffmann-LaRoche, Inc.

From the Myasthenia Gravis Clinic, Massachusetts General Hospital and the Department of Neurology, Harvard Medical School. Paper number five.

Read before the Section on Nervous and Mental Diseases at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 17, 1939.

1. Willis, Thomas: De Anima Brutorum, London, 1672, p. 288.

2. Erb, Wilhelm: Zur Casuistik der bulbären Lähmungen: 3. Ueber einem neuen, wahrscheinlich bulbären Symptomencomplex, Arch. f. Psychiat. **9**: 336-350, 1878.

3. Goldflam, S.: Ueber einen scheinbar heilbaren bulbärparalytischen Symptomencomplex mit Betheiligung der Extremitäten, Deutsche Ztschr. f. Nervenh. **4**: 312-352, 1893.

4. Jolly, F.: Pseudoparalysis myasthenica, Neurol. Centralbl. **14**: 34-36, 1895; Myasthenia gravis pseudoparalytica, Verhandl. d. Berl. med. Gesellsch. **25**: 249-250 (part 2) 1895.

5. Edgeworth, Harriet: A Report of Progress on the Use of Ephedrine in a Case of Myasthenia Gravis, J. A. M. A. **94**: 1136 (April 12) 1930; The Effect of Ephedrine in the Treatment of Myasthenia Gravis: Second report, ibid. **100**: 1401 (May 6) 1933.

6. Boothby, W. M.: Myasthenia Gravis: A Preliminary Report on the Effect of Treatment with Glycine, Proc. Staff Meet., Mayo Clin. **7**: 557-562 (Sept. 28) 1932. Boothby, W. M., and others: Myasthenia Gravis: Second Report on the Effect of Treatment with Glycine, ibid. **7**: 737-756 (Dec. 28) 1932.

7. Walker, M. B.: Treatment of Myasthenia Gravis with Physostigmine, Lancet **1**: 1200 (June 2) 1934; Case Showing Effect of Prostigmine on Myasthenia Gravis, Proc. Roy. Soc. Med. **28**: 759 (April) 1935.

8. Pritchard, E. A. Blake: Prostigmine in the Treatment of Myasthenia Gravis, Lancet **1**: 432 (Feb. 23) 1935.

9. Pritchard, E. A. Blake, and Walker, M. B.: The Effect of Prostigmine on the Symptoms and on the Myogram in Myasthenia Gravis, J. Physiol. **84**: 35 P (May 13) 1935.

10. (a) Viets, H. R., and Schwab, R. S.: Prostigmine in the Diagnosis of Myasthenia Gravis, New England J. Med. **212**: 1280-1283 (Dec. 26) 1935. (b) Viets, H. R., and Mitchell, R. S.: The Prostigmine Test in Myasthenia Gravis: Second Report, ibid. **215**: 1064-1065 (Dec. 2) 1936. (c) Schwab, R. S., and Viets, H. R.: The Prostigmine Test in Myasthenia Gravis: Third Report, ibid. **219**: 226-228 (Aug. 18) 1938.

11. Harvey, A. M., and Whitehill, M. R.: Prostigmine as an Aid in the Diagnosis of Myasthenia Gravis, J. A. M. A. **108**: 1329-1333 (April 17) 1937.

12. Gammon, G. D., and Scheie, Harold: Use of Prostigmine as a Diagnostic Test of Myasthenia Gravis, J. A. M. A. **109**: 413-414 (Aug. 7) 1937.

13. Everts, William H.: The Treatment of Myasthenia Gravis by the Oral Administration of Prostigmine, Bull. Neurol. Inst. New York **6**: 523-530 (Dec.) 1935.

14. Viets, H. R., Mitchell, R. S., and Schwab, R. S.: The Oral Administration of Prostigmine in the Treatment of Myasthenia Gravis, J. A. M. A. **109**: 1956-1959 (Dec. 11) 1937.

15. Boothby, W. M.: Myasthenia Gravis: Eighth Report, Tr. A. Am. Physicians **51**: 188-198, 1936.

16. Kennedy, F. S., and Moersch, F. P.: Myasthenia Gravis: A Clinical Review of Eighty-Seven Cases Observed Between 1915 and the Early Part of 1932, Canad. M. A. J. **37**: 216-223 (Sept.) 1937.

The diagnosis of myasthenia gravis is usually not difficult from the history and the clinical examination. The Jolly reactions were found to be of moderate assistance in diagnosis but proved to be not so valuable as the ergographic examination, especially in cases of general muscular weakness. In the ergograph test the

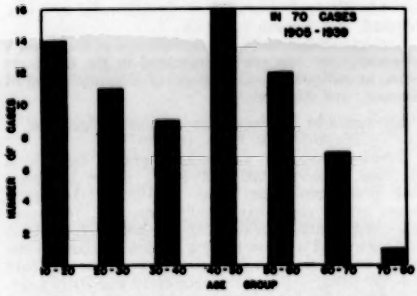

Fig. 2.—Age at onset of symptoms in the seventy cases.

muscles are exhausted by repeated pressure on a bulb, an observation easily recorded on a moving drum (fig. 4). Similar curves may be recorded in an electromyogram, as reported by Lindsley,[17] who examined some

TABLE 1.—*The Prostigmine Test*

Time, Minutes	Objective Improvement	Subjective Improvement
10	0	0
20	0	½
30	0	1
40	1	0
50	0	0
60	0	0
	1	1½
Total		2½

Negative Test: Progressive Bulbar Palsy

Time, Minutes	Objective Improvement	Subjective Improvement
10	2	2
20	4	4
30	4	4
40	4	4
50	3	4
60	3	3
	20	21
Total		41

Positive Test: Myasthenia Gravis

of our patients. The most efficient test for the disease, particularly useful for patients with few symptoms, is the "prostigmine test," as reported in previous communications.[10] The results are quickly tabulated (table 1). By careful evaluation of the results, diseases such as psychoneurosis and numerous neurologic conditions giving rise to ptosis, diplopia, dysphagia, dysarthria and general muscular weakness are eliminated. The test has proved in our hands to be a valuable diagnostic procedure. In addition, for patients with dysphagia, fluoroscopic examination has been helpful (fig. 5), the barium sulfate being observed both before and after the injection of prostigmine. Chemical studies have not been helpful in diagnosis, as was the case in Boothby's long series.[18] We have been unable to associate myasthenia gravis with enlargement of the thymus gland. All roentgenlogic studies failed to reveal such enlargement, and in two cases air injected into the mediastinal cavity failed to show the gland in the roentgenograms. This was surprising in view of the report of Norris,[18] who observed hyperplasia of the thymus in 50 per cent of his four patients examined post mortem and found an equal incidence in the literature.

THE TREATMENT OF MYASTHENIA GRAVIS SINCE 1935

Treatment with intramuscular injection of prostigmine methylsulfate was begun in 1935, but after the report of Everts[13] prostigmine bromide for oral use

TABLE 2.—*Dosage Schedules of Prostigmine Given Orally*

Average Involvement; Prostigmine and Ephedrine

	A. M. 7	8	9	10	11	12	P. M. 1	2	3	4	5	6	7	8	9	10	10 p.m. to 7 a.m.
Prostigmine		1		1			1			1		1		1			
Ephedrine		1					1					1					

Severe Involvement; Prostigmine and Potassium Chloride

	A. M. 7	8	9	10	11	12	P. M. 1	2	3	4	5	6	7	8	9	10	10 p.m. to 6 a.m.
Prostigmine		2		2			2			2		2		2			
Potassium chloride		1					1					1					

Severe Atypical Involvement; Prostigmine, Belladonna Drops, Ephedrine and Scopolamine

	A. M. 7	8	9	10	11	12	P. M. 1	2	3	4	5	6	7	8	9	10	10 p.m. to 7 a.m.
Prostigmine			1		2			1			2				1		2
Belladonna					3						3						3
Ephedrine					1						1						1
Scopolamine			½				½					¼					

Successful Medication with Prostigmine and Guanidine

	A. M. 7	8	9	10	11	12	P. M. 1	2	3	4	5	6	7	8	9	10	10 p.m. to 7 a.m.
Prostigmine		1								1				1			
Guanidine hydrochloride	1						1				1				1		

was soon substituted. We began by using the drug cautiously, having in mind the experience reported by Goodman and Bruckner.[19] As noted in our previous

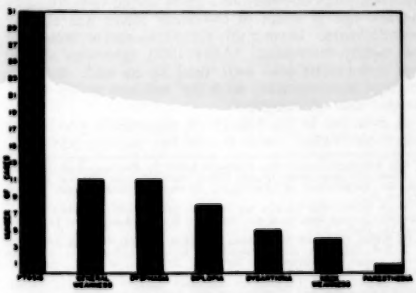

Fig. 3.—Presenting symptoms in the seventy cases.

paper,[14] the warning was not needed if one dealt only with myasthenia gravis and did not give large doses to normal persons. The drug may even be given in daily doses of from twenty to twenty-five pills of 15 mg. each

17. Lindsley, D. B.: Myographic and Electromyographic Studies of Myasthenia Gravis, Brain **58**: 470-482 (Dec.) 1935.

18. Norris, E. H.: The Thymoma and Thymic Hyperplasia in Myasthenia Gravis with Observations on the General Pathology, Am. J. Cancer **27**: 421-433 (July) 1936.

19. Goodman, L. S., and Bruckner, W. J.: The Therapeutics of Prostigmine, J. A. M. A. **108**: 965-968 (March 20) 1937.

without serious results in severely affected patients. More important than the size of the dose, however, is the spacing of the drug throughout the twenty-four hour period. We found useful a prescription form on which the hours of the day were numbered, so that the dose could be accurately regulated. The schedule is

Fig. 4.—Ergograms in a case of myasthenia gravis taken before and after the use of prostigmine was begun.

given to the patient, a duplicate being retained. Typical schedules show a wide variety of spacing and dosage, as well as the other drugs used with prostigmine (table 2).

Regulation of the dosage was not by any means easy, and two groups of patients presented particular difficulties. The first group consisted of patients with severe involvement, with dysphagia and dysarthria as the presenting symptoms. For these large doses of the drug were necessary, from ten to twenty pills of 15 mg. each daily, in order to obtain a maximum effect. The patients in the other group, a smaller one, were sensitive to prostigmine and required small doses, 7.5 mg., spaced widely throughout the day. Once the dosage was regulated so that the patient was getting the maximum effect throughout the day and night, no change was necessary for months and no increased tolerance or disagreeable

TABLE 3.—*Value of Various Forms of Prostigmine Therapy Used in Forty-Four Cases of Myasthenia Gravis, 1935-1939*

		Evaluation			
	Cases	Zero	Poor	Fair	Good
Oral administration	44		2	2	40
Subcutaneous injection	8			2	6
Administration of enteric coated tablets	8			4	4
Use in suppositories	8			2	6
Use in eyedrops	2		2		
Inhalation of powder	4	4			

effects from accumulation of the drugs was observed. The regulation of the dosage required some weeks or even months, and for this reason our patients were seen at weekly intervals. After the patient was satisfactorily adjusted to his medicine, we interviewed him once every four to eight weeks.

Because of the high cost of prostigmine, we endeavored to find a more potent form for oral administration. About ten times as much for oral as for intramuscular administration is required to give the desired effect. We tried enteric coated prostigmine, prostigmine eye drops, suppositories of prostigmine and inhalations of prostigmine powder (table 3). Enteric coated tablets do not materially affect the value of prostigmine. The drug may be given successfully by suppository but not by eye drops or powder inhalations. Oral and parenteral administration are therefore the methods of choice.

Various drugs may be used to increase the effects of prostigmine. Many were tried in constantly changing doses and amounts (table 4). The most useful was ephedrine sulfate, a drug having by itself a definite effect on myasthenia gravis. Ephedrine increased the effect of the prostigmine in forty-one of forty-three cases and failed in only two. Aminoacetic acid, contrary to our expectations from Boothby's reports,[19] proved to be of no value in seventeen cases. As much as 45 Gm. a day in divided doses, a larger amount than Boothby recommended, was given.

TABLE 4.—*Drugs to Increase the Effect of Prostigmine*

		Evaluation			
	Cases	Zero	Poor	Fair	Good
Ephedrine sulfate	43	2		2	39
Benzedrine sulfate	5	1		2	2
Doryl (orally)	5	5			
Mecholyl (subcutaneously)	3	2	1		
Aminoacetic acid	17	17			
Guanidine (orally)	25	17	2	2	4
Potassium chloride	15	5		4	6
Vitamins	7	2	2	3	
Endocrine preparations	4	4			
Pregnancy	4	1			3

TABLE 5.—*Mortality Figures*

	Over 50 Years	Under 50 Years	Total
Number of patients	18	26	44
Number of deaths	4	1	5
Percentage of deaths	22	4	11.6

After the work of Minot,[20] twenty-five of our patients received guanidine orally, alone or with prostigmine, a variety of guanidine salts being used. Guanidine carbonate was the most satisfactory compound, but the hydrochloride was about as effective. Guanidine increased the effect of prostigmine in eight of twenty-

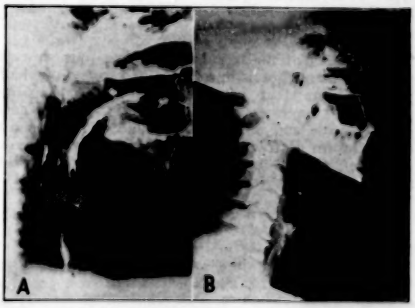

Fig. 5—Fluoroscopic study with barium sulfate in a case of myasthenia gravis with marked dysphagia. *A* was taken before and *B* after the use of prostigmine was begun.

five cases. In four the results were good. Seventeen other patients, however, failed to respond to guanidine. Potassium chloride in doses of 20 Gm. a day, given in a 25 per cent solution, was effective in reducing the intake of prostigmine in cases of severe involvement.

20. Minot, A. S.; Dodd, Katharine, and Riven, S. S.: The Response of the Myasthenic State to Guanidine Hydrochloride, Science **87**: 348-350 (April 15) 1938.

Of fifteen patients using potassium chloride with prostigmine, there was a decided benefit in ten. Vitamin and endocrine treatments were not helpful. Three of our patients, however, were improved during pregnancy; one was worse.

RESULTS OF THE ORAL THERAPY WITH PROSTIGMINE

Forty-four patients in our clinic have now been taking prostigmine orally for from a few months to two and one-half years (fig. 6). Thirty-one have taken the drug more than one year and nine more than two years. During this period (1935-1939) there have been five deaths, four of patients over 50 years of age and one of a patient aged 27 (table 5). The mortality figures indicate that of eighteen of our patients over 50 years of age, 22 per cent have died. One of the twenty-six patients under 50 (4 per cent) died of the disease. In the older group, two died of causes incident to age and the other two failed to take prostigmine consistently. The younger patient died of myasthenia gravis in spite of adequate treatment. Her pathologic examination will form the subject of a later communication. No gross thymic tumor was found.

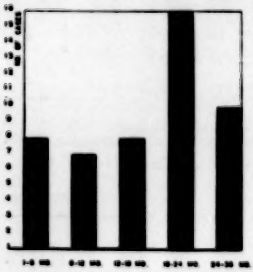

Fig. 6.—Duration of treatment in forty-four cases of myasthenia gravis, 1935 to 1939.

Remissions have occurred in seven cases, so that prostigmine is no longer required. This is a somewhat larger percentage than might be expected in the natural course of the disease in forty-four patients with various types of myasthenia gravis. Five patients, moreover, have been able to reduce their intake of prostigmine.

CONCLUSION

The results of the treatment of forty-four patients with myasthenia gravis in a period of two and one-half years indicate that prostigmine bromide taken by mouth and supplemented with ephedrine sulfate, potassium chloride and occasionally guanidine is the most efficient form of treatment for myasthenia gravis now available. Of the forty-four patients, five have died and seven have shown full remissions.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. MINOT, DODD AND RIVEN AND DRS. VIETS AND SCHWAB

DR. J. C. MCKINLEY, Minneapolis: Myasthenia gravis is a disease which can now be removed from the category of hopelessness and almost invariable fatality to that of reasonable well-being and markedly improved life expectancy, thanks to the group of investigators to which the previous speakers belong. That the problem is not yet completely solved is indicated, however, by deaths in the series of Drs. Viets and Schwab in spite of treatment which they considered optimal. Then too, in both papers reference has been made to such puzzling observations as the variability in response to prostigmine and guanidine and the occurrence of true remissions in a certain proportion of myasthenic patients with or without therapy. Presumably insight into questions of this sort will be gained as our understanding of the metabolic mechanisms of muscle tissue improves. The recent advances in the therapy of myasthenia are a stimulus to thinking and, therefore, to clinical, physiologic and chemical research. To my mind this is a by-product of major importance. Drs. Viets and Schwab have referred to the occurrence of remissions in seven of their forty-four patients under prostigmine therapy. They state that this represents a somewhat larger percentage of remissions than might be expected in the natural course of the disease. One cannot take issue with this as a statement of raw fact, but in reading it unmodified one can scarcely avoid the inference that prostigmine was somehow responsible for producing some of the remissions in treated cases. That is only my reaction. Possibly such an inference is actually correct. With no desire to be hypercritical of the splendid work of the writers, I feel that on this point they are vulnerable to criticism on statistical grounds. It is apparent that a shift of one or two, or possibly three, cases into or out of the group of the remissions could easily occur by chance in another series in the process of random sampling. This would markedly alter the percentage of remissions. The reference to an increase in the remission rate under treatment is thus not valid unless the differences can be shown to have statistical significance.

DR. S. S. RIVEN, Nashville, Tenn.: My association with Dr. Minot and Dr. Dodd is that of a clinician, and I have been following these patients. We do not know yet how guanidine brings about the prompt, temporary improvement in myasthenia. We are not certain as to the mechanisms involved in the action of prostigmine. The two therapeutic agents may or may not work through the same mechanism. Certainly with respect to their action on cholinesterase activity the two drugs are quite dissimilar. Concentrations of prostigmine as low as one part per million completely inhibit esterase activity, while guanidine in amounts as great as one part per hundred, a level hundreds of times as high as can be maintained in vivo, has no effect whatever on the activity of this enzyme. We do not yet understand the basis of the greatly increased tolerance for guanidine on the part of myasthenic patients. We have shown experimentally that they do not merely excrete it faster than normal individuals, nor does its administration cause an increased excretion of either creatine or glycocyamine in the urine. Further than that we cannot say at present. The fact that calcium salts were shown in the earlier work of Dr. Minot to control the increased muscle tone and tremors induced by toxic amounts of guanidine, together with the observation that occasionally potassium enhances the effect of guanidine in myasthenia, suggests that changes in salt equilibrium may be of fundamental importance. There are one or two clinical facts that I should like to emphasize. Not a single patient in our series showed any spontaneous remission. A dose of guanidine which produces a toxic effect in a normal individual causes no undesirable symptoms in patients with myasthenia gravis. It seems that patients with myasthenia gravis respond to guanidine as pernicious anemia patients respond to liver.

DR. ANN S. MINOT, Nashville, Tenn.: I think that our experiences and Dr. Schwab's experiences indicate that guanidine probably has a place in the symptomatic treatment of myasthenia gravis. I do not think it is a cure of the underlying condition. Perhaps the greatest interest from the physiologic point of view is that each new drug that brings about a response in this disease gives us a new tool, a new method of approach to a condition about the cause of which we know nothing. If we can get several angles of approach, I hope that perhaps from this work we may get a better understanding of the condition itself and of the essential features of successful therapy.

DR. HENRY R. VIETS, Boston: I think that neither of these papers can be considered as final in any sense of the word. They are merely progress reports. We knew little about myasthenia gravis even five years ago, although the disease had been adequately described. In the last five years we have had the opportunity to observe closely forty-four cases of myasthenia gravis. We are learning something about the disease and the methods of controlling it. I think we have no statistics that are really of any value in regard to remissions. Our statement that seven of our patients out of forty-four were now in remission appears to be a figure that, when compared with the literature, is larger than has been noted before. We have no real basis of comparison, however, because of the thirty patients

who were observed at the Massachusetts General Hospital from 1905 to 1935 seven died in the hospital or almost immediately after leaving it. The evidence is that probably a great many of the others died within a year or two. A fair conclusion to draw with regard to remissions is that we now have drugs, such as guanidine, prostigmine and ephedrine, that carry patients through serious attacks of myasthenia gravis, even preventing death, and, therefore, permit them to recover to a state where remission is possible. If that is so, we are saving a large number of patients who previously would have succumbed to the disease. Certainly, of the forty-four patients whom we have observed, at least one third and perhaps one half would have died within a year or two after they were first seen, without the beneficial effect of ephedrine, guanidine and prostigmine.

HISTORICAL NOTES ON CORONARY OCCLUSION: FROM HEBERDEN TO OSLER

FRANK BILLINGS LECTURE

GEORGE DOCK, M.D.

PASADENA, CALIF.

In the Section on Practice of Medicine I have had the honor of acting as secretary, chairman and orator, no doubt by the active intervention of Frank Billings; but the Frank Billings Lectureship is so special a distinction that I cannot adequately express my appreciation of the honor. I enjoyed Frank Billings's friendship for a long time and realized his rare personality, his unusual genius as practitioner, consultant, teacher and leader of far reaching influence, and one of the most stimulating factors in the growth of the scientific element in the American Medical Association.

In selecting a topic worthy of the occasion I was moved by long-standing interest in the subject and also by recalling the part played by many of my friends and Billings's pupils and associates in the investigation of the physiology and pathology of the coronary arteries, and especially by the long continued and successful work of James B. Herrick. Three years ago George Blumer gave a model study of one form of coronary disease. As new material accumulates we tend to forget the early history of a subject, and as there are still lessons to be learned from that I decided to give a short essay on some of the chief incidents of coronary study from the time of Heberden to that of Osler.

TERMINOLOGY

The coronary arteries were looked at before the time of Heberden; alterations were described and some symptoms noted, but the former remained as anatomic curiosities and all were buried until more inquisitive times. By giving to a group of symptoms a euphonious name that has survived until now, William Heberden (1768) opened a new chapter in nosography, and so the name deserves a brief consideration. "Angina" as a technical term came down from classic times, and for almost two centuries before Heberden it was used in England to designate cases of quinsy or sore throat in which a feeling of strangling and anxiety entered. "Chest pang" was therefore an apt name for the syndrome that arrested Heberden's attention. No theory was suggested, and the seat was indicated only in a general way. Those who use the Oxford Dictionary may think I err in giving Heberden priority, because that great storehouse of words gives a reference to "1744, Walls, on the Angina pectoris." I was unable to find the reference in the *Philosophical Transactions* and wrote to the Clarendon Press for information. A prompt and courteous reply stated that the date 1744 "rests on no foundation" but that in the "Medical Tracts of John Wall," published in 1780, is a letter to Dr. Heberden "On the Angina Pectoris." Angina was used in Germany at the same early period for cases of sore throat or croup, probably including diphtheria, and continued to the present time, extended with the recognition of leukopenic sore throat. Soon after Heberden's first article Germans translated his name for the disease as "brustbraeune," "browny" being an old technical term for the common anginas, and although it was promptly criticized by informed writers it persisted for many years. Objections to Heberden's term brought forth many substitutes, most of which did not long survive and need not be recalled. Parry proposed syncope anginosa, although syncope was not a frequent symptom or when it seemed present was sometimes the passage into death. "Stenocardia," proposed by Brera (1810), was objected to as arising from an erroneous conception of the nature of the disease but has been used down to the present time, especially in Germany, and is often useful as an adjective.

The coronary arteries entered medical thought and literature with the belief held by a brilliant group of English medical men, Edward Jenner, John Hunter, John Fothergill and Caleb Hillier Parry, that those vessels were closely associated with angina pectoris, and their view was quickly adopted by some of the leading physicians of Europe, especially Kreysig, whose three volume work on Diseases of the Heart appeared from 1814 to 1817, and by Brera (1810) and Testa (1810) in Italy. In 1809 Allen Burns published "Observations on Some of the Most Frequent and Important Diseases of the Heart." In the chapter entitled "Observations on Disease of the Coronary Arteries, and on Syncope Anginosa," he agreed with Parry as to the importance of cardiac ischemia but did not attempt to settle the question whether in angina the heart is in a state resembling paralysis or in a spasmodic contraction.

The attitude of early French authorities has troubled later writers. Corvisart did not make a definite statement about angina pectoris or the coronary arteries in that condition. But the work of Corvisart on the heart is not a textbook or monograph on modern lines. It is a collection of lectures entitled "Essay on the Diseases and Organic Lesions of the Heart and Great Vessels," taken from Corvisart's clinical lectures and prepared by an editor, C. E. Horeau, first printed in 1806 and republished several times later. In the chapter on Rupture of the Heart a number of cases are cited, including some that may have been due to infarcts in angina subjects, but without sufficient detail. Incidentally, the "aneurysm of the heart" of Corvisart was not what we now call aneurysm or partial aneurysm but dilatation. The heterodox views of Laënnec include two classes of ideas, one a matter of classification, the other that of clinical observation. As to the first, he classified angina pectoris as a nervous disease. At that time nervous diseases were even less understood than were diseases of the heart. Laënnec, even as an undergraduate, was a pioneer in pathologic anatomy, and he wrote the chapters on that subject in the "Dictionnaire des sciences médicales," just beginning its series of

Read before the Section on Practice of Medicine at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 17, 1939.

sixty volumes. In volume 2 (1812) he divided all diseases into two classes. "First, those accompanied by an obvious lesion in one or many organs, hence called, for some years, organic diseases; second, those which show no constant lesion in any part of the body from which their origin could be derived. These are commonly called nervous diseases." He continued: "If one is called to a patient with an affection of the thorax in which dyspnea is the principal symptom and where one finds no signs indicating pulmonic phthisis, a disease of the heart, an aneurysm of a great vessel, or any other organic affection of the parts contained in the thorax, one can conclude that the disease is nervous." In volume 2 of the Traité de l'auscultation médiate," 1826, page 744, he designated nervous disorders of the heart and great vessels, including neuralgia of the heart, nervous palpitation, spasm of the heart with bellows murmur and fremitus, nervous disorders of the arteries, spasm of the arteries with murmur and fremitus. The section on Heberden's angina pectoris begins on page 745 under the heading Neuralgias of the Heart. He was familiar with the symptoms, especially of the mild forms, but we are surprised when he tells us that he opened many bodies in angina cases without finding the coronary arteries ossified, the term then used for arteries stiffened by sclerosis. But we cannot understand any more than when under treatment he tells us of the good results he had from placing two magnetized steel plates over the front and back of the patient.

APPLICATION OF PHYSICAL DIAGNOSTIC METHODS

The real study of heart disease began only after percussion had been applied in diagnosis and Laënnec had shown the scope of auscultation. When that was done a period of active application of physical diagnostic methods began and the steady round of discoveries in the diagnosis and pathology of valvular disease may have diverted attention from the less objective signs of angina pectoris. At all events, interest in the coronary arteries waned and interpretations of angina as a nervous disease began to multiply, although the real study of diseases of the nervous system had hardly passed the stage it was in while Laënnec was alive. Some of the arguments against the coronary theory of angina pectoris seem very weak now. One of the most popular was that coronary disease was often present without angina, and this was used with such a feeling of finality that it might serve as a warning in many clinical puzzles. Often the coronary arteries were not examined or if so in a very casual manner, and the statements as to ossification do not describe the real condition of the wall or the surface of the intima over a thickening. We know that in some cases there were rough spots on the intima where platelets might settle and be followed by fibrin formation, with danger of thrombosis or embolism at some time later, in one of many varieties of size and location. Also in many such bodies the subjects had missed the danger of a coronary accident by dying early, and if they had lived even a short time more might have had an attack of angina, an infarction with recovery or a rupture of the ventricle. From time to time a more thoughtful observer published a suggestive report, but with no impression on the opinion of the time.

THE PERIOD OF EXPERIMENTATION

The next period in the development of the study of coronary disease, that of experiment, began with a suggestion by Dr. Marshall Hall, best known for the discovery of reflex action but recognized in his lifetime as a wise practitioner and a keen and versatile physiologist. In the Gulstonian Lecture in 1842 he took as his subject "The Mutual Relations Between Anatomy, Physiology, Pathology, and Therapeutics, and the Practice of Medicine." One section was headed "The Coronary Circulation; Sudden Death." Referring to Bichat's "tripod of life," he stressed the importance of sudden death due to arrested coronary circulation. He said that ossification of the coronary arteries or "a substance resembling cartilage in the walls" of those vessels was the common cause of syncope and death. He had proposed to himself to test the problem by arresting the circulation by ligation or by the injection of solid substances into the coronary arteries, and he gave details of the methods to be used.

In the same year the young surgeon famous later as Sir John Eric Erichsen reported some experiments. In dogs and rabbits he passed ligatures by curved needles around the coronary arteries and found that he could cause a speedy cessation of the heart's action. This work was referred to by many later writers, but no control was attempted for another twenty years. In 1862 Prof. P. L. Panum, then in Kiel and recognized as a brilliant physiologist, published "Experimentelle Beitraege zur Lehre von der Embolie," an extensive study based on Virchow's epoch-making investigation on embolism. Panum had witnessed some of Virchow's experiments and he began his work in the hope of enlarging discoveries already made. He thought his observations gave reason for doubting Virchow's belief that lack of arterial blood in the coronary arteries was a cause of death and that "angina cordis seu pectoris" could be the result of embolism of those vessels, but he did not deny that sudden death might follow obstruction of the coronary artery. He knew of Erichsen's experiments only through Virchow's reference to them and was uncertain how early the heart stopped or whether other circumstances altered the results of the operation. He wished to make some ligations but thought it impossible to do so on the moving hearts of live animals. It was then that he spread the case of Thorwaldsen beyond the Danish language. The celebrated sculptor died suddenly in the theater and, post mortem, atheroma and calcification were found and an atheromatous abscess in the anterior coronary artery, which had burst into the lumen, filling the latter with its soft contents. Dr. Fenger, who had assisted at the autopsy, wrote to Panum saying that he thought the interruption of the circulation through the coronary artery had lamed the muscle and so led to death. Panum commented: "The probability cannot be denied, but the facts are not convincing. For we do not know when the atheroma burst, immediately or hours before the death struggle. Also, there are no data on the histological condition of the muscle fibers. If they were fatty degenerated, as is not improbable, the cardiac paralysis might be due to the same cause, admittedly unknown, that so frequently leads to death in cases of fatty heart without participation of the coronary arteries. Finally, no one can tell the behavior of the heart during the death struggle, which might have lasted minutes rather than seconds." One must admire Panum's skepticism. He clearly recognized the complexity of experiments on coronary arteries but did not realize the meager knowledge of cardiac physiology and pathology at the time, and his experimental embol-

V 19

isms did little to enlarge them. It is interesting to know that he died of ruptured left ventricle at the age of 65.

The next experimenter was another prominent physiologist, Albert von Bezold, professor in Würzburg. In the course of a long series of studies on the heart and circulation (1863-1867) he examined changes in the heart beat after compression of the coronary arteries in some twenty rabbits. In most cases the operation had no immediate effect on the pulse rate; if any, it became slow rather than fast. In short, von Bezold did not agree with Virchow that obstruction of the coronary artery could cause fatal asphyxia. In all the early experiments associated phenomena were overemphasized, and discussions about them diverted attention from the main topic.

Dr. B. Samuelson of Königsberg (1881) made experiments suggested by the case of a man who had focal brain symptoms (syphilitic), recovered after treatment but then had "asthmatic attacks" attributed to fatty heart largely because he was obese. After five years of freedom from symptoms he went into collapse, with a pulse rate of 35, and died in five hours. Autopsy revealed sclerotic coronary arteries, the lumen almost obliterated and no fatty degeneration. Samuelson made experiments after von Bezold's method, with the assistance of the physiologist Professor Gruenhagen. Even with complete occlusion he got no immediate cessation of heart action, and death followed only long continued or repeated obstruction. Following obstruction he found, among other changes, enormous swelling of the left auricle, relieved by loosening the ligature but never recovering completely. He thought that the mechanism after artificial occlusion must be the same as in angina pectoris; that the swelling explained the substernal pain, while the altered heart action, weak pulse, pallor and cold extremities went far to account for the anxiety. He admitted that sclerosis of the coronary arteries did not fully explain angina pectoris and agreed with Parry and Stokes that the symptoms of the latter were due to transitory weakness in a heart already weak. Divergent results in animal experiments he explained by differences in strength.

The next important experiments were made by Julius Cohnheim and Anton von Schulthess-Rechberg (1881). Cohnheim had an unusually sound physiologic point of view and he had practiced in Carl Ludwig's laboratory the methods used in work on the circulation. Instrumental assistance was carried out more fully than in previous attempts. Cohnheim premised by stating that pathologists had shown that an examination of the heart was incomplete unless the coronary arteries were minutely scrutinized and that since that had been accepted many diseases of the heart formerly called idiopathic had been shown to be the results of coronary disease, especially "fatty degeneration," "fibroid myocarditis" and aneurysmal dilatation of the left ventricle. Many good observers considered neuralgia of the heart, angina pectoris and sudden death as coronary effects, but as the matter was still unsettled he undertook the experiments described. He selected dogs on account of the superficial course of the coronary vessels in those animals, with branches much like those in man, and rather large dogs. He convinced himself that the arteries were end arteries and so lent themselves to obstruction of definite areas, although he did find one anastomosis in a large number of dogs. He realized the differences between human arteries with chronic thickening and those of lower animals with artificial occlusions, and he knew that in human subjects circulation may proceed even with a certain reduction of lumen and that, if sudden obstruction occurred, something new must have happened. He recalled that in the brain acute softening takes place in areas where the arteries are thickened and calcified. A minimum of blood suffices for function to continue, but unusual exertion or emotional strain makes demands too great for the supply. It is not necessary to describe the details of his experiments. There was no effect in less than thirty or forty seconds after ligation. Then the pulse became intermittent, then frequent, followed by slowing and a sudden arrest of both ventricles in about 105 seconds. The auricles continued to beat, but feebly, and the ventricles began a "wallowing" or fluttering motion. Swelling of the auricles was transitory, if it did occur. Contractions did not return after ligatures were removed. Cohnheim thought he could exclude vagus participation. He discussed the possibility of a heart poison, interesting now but chimerical at that time. He also gave a comparison of experimental and clinical conditions following occlusion.

Another experimental study was made by an accomplished young American physiologist, W. T. Porter (1892-1896). His results did not differ essentially from those of Cohnheim, but he clarified the end artery problem, showing that "not the absence but the character of the anastomosis is the basis of the present teaching in pathology" and that "the idea of terminal arteries is physiological, not anatomical."

Soon after Roentgen's discovery a pupil of Porter, Dr. Walter Baumgarten of St. Louis (1899), made a contribution to the application of x-rays to the coronary arteries.

About the same time as Porter's early work, Dr. Rudolf Kolster (1893) of Helsingfors reported the results of a series of experiments in which small branches of the left coronary artery were ligated and the occluded areas examined at intervals of from one day to more than a year. The results agreed to a striking degree with observations after accidental infarction.

WORK OF THE PATHOLOGISTS

The later experimental work confirmed the beliefs of Jenner, Parry and their followers and brought the subject of coronary obstruction definitely into pathology. Before taking up the work of pathologists it will be useful to consider the views of some great clinicians of the nineteenth century. Stokes (1855) said: "We may conclude that the special group of symptoms described as angina pectoris . . . is but the occurrence, in a defined manner, of some of the symptoms connected with a weakened heart. Obstruction of the coronary arteries may or may not be present and is probably not infrequent, but as a cause of angina its action is remote and its existence unnecessary. It is only by causing atrophy with fatty degeneration, as Dr. Quain has shown, that it appears remotely to produce angina." He compared the heart in angina to an intestinal tube with ileus and also suggested overdistention of collateral vessels as an explanation of the pain. He had never seen the severe form of angina described by Latham or the purely nervous cases of Laënnec. He thought that cases most often called angina might be more properly designated cardiac asthma, and he suggested useful clinical and anatomic methods for the better study of cases. Trousseau

(1873) called angina pectoris "this singular neuralgia" but was aware of the variety of lesions found with it. The English translation of Ziemssen's Encyclopedia, nineteen volumes, 1874-1879, was a great stimulus to medical thought in the United States. The Index of the Heart volume does not contain the words angina pectoris, stenocardia or coronary artery, but the latter is mentioned (vol. VI) as the cause of rupture of the heart. Angina pectoris is treated under Diseases of the Nervous System in volume XIV, page 31. Senac, Corvisart and other early writers are quoted to controvert the coronary theory, and angina pectoris is described as a definite disturbance of the innervation of the heart. Austin Flint, whose textbook was so justly admired by Dr. Osler, in his 1881 edition said that angina pectoris involves, as an essential feature, neuralgia and might be included among diseases of the nervous system. "It has been observed," he said, "in cases in which the coronary arteries are obstructed by calcification or other lesions, but obstruction of these arteries is not essential to its occurrence, as was at one time supposed." His chapter is still worth reading for its clinical details. A few years later, in the chapter on Angina Pectoris in Pepper's System of Practical Medicine (vol. 3, 1885), Flint said "The pathological condition on which the angina depends is ischemia of the heart" and he named coronary disease as the probable basis. For the explanation of the pain he referred to the intense pain in the limb which follows embolism of the femoral artery. It seems certain that Dr. Flint's later views were influenced by his association with Dr. W. H. Welch, pupil of Cohnheim and close friend of Carl Weigert. The author of the section on diseases of the coronary artery in Pepper's System (vol. 3, p. 828) said it was "doubtful if a diagnosis could be arrived at."

The earliest examinations of the heart after death in angina were made by physicians and surgeons, and in some cases, as Corvisart's editor said, made hurriedly and often clandestinely. The microscope was not applied to such work until the middle of the nineteenth century, which explains the long continued reference to ossification of the coronary arteries. A new era began when the great pathologists of the nineteenth century, making formal autopsies, turned their attention to coronary and myocardial disease. Cruveilhier (1842) saw infarcts, as did Rokitansky (1856). Virchow expressed himself briefly but explicitly, as I have mentioned.

An interesting contribution to coronary pathology was made by H. Boettger, an asylum physician, in 1863. Having seen two examples of rupture of the heart, Boettger collected and analyzed reports of sixty-two cases. In thirteen cases coronary disease had been noted; the lesions included varices, atheroma and thrombosis. Healing occurred only after adhesions. Death was often sudden, but duration up to eighteen hours was observed. Often there was no warning—a fall, loss of consciousness, and death in a few seconds. Sometimes, before the fall, there was an anxious cry, and in twenty-one of thirty-four cases there were prodromal symptoms suggesting angina pectoris. Pain varied from dull pressure under the sternum to unbearable pain in the same region or in the left hypochondrium, left shoulder or left arm.

This contribution seems noteworthy now, but it did not definitely influence thought at the time and there was no distinct advance until Carl Weigert (1880) opened a new era in pathology by setting up the conception of coagulation necrosis and by improvements of histologic staining. In his article "Ueber die pathologischen Gerinnungsvorgaenge," after speaking of renal infarcts, Weigert said: "Still more typical, perhaps, is another kind of infarction which strangely enough has not been at all considered (beachtet): infarcts of the heart muscle." He continued, and it is worth while to quote his words, "In atheromatous changes of the coronary arteries, not infrequently thrombotic or embolic obstructions form in the branches of the arteries. If the obstruction forms slowly, or at least in such wise that collateral channels exist, but not enough to keep up nutrition, a slow atrophy occurs with destruction of the muscle fibers without injury to the connective tissue. The muscle fibers that disappear are replaced by fibrous connective tissue, and the so-called chronic myocarditis is nothing else than such a process. We cannot speak of a disappearance of muscle fibers by 'compression of an inflammatory exudate' or by 'contraction of new-formed connective tissue masses.'" It is interesting that, although the principles of infarction and subsequent repair were quickly accepted by pathologists, "chronic myocarditis" continued to be used in textbooks on medicine and in clinical work generally just as it was when such processes were supposed to be of inflammatory origin. It would seem if we must continue "-itis," that we should abandon the old connotation and think of fibrosis rather than inflammation.

About the time Weigert was explaining infarction, Prof. Ernst Ziegler (1880), then in Tübingen, later in Freiburg, proposed "myomalacia cordis," softening of the heart, after the analogy of "encephalomalacia" or softening of the brain. He described the details in his widely used textbook with adequate references to the historical development of the subject, showing that the process was recognized by several authors although overlooked or misinterpreted by many.

Weigert in his article said that his colleague Karl Huber would report a series of cases, and that was done in 1882 in *Virchows Archiv*. Huber gave abstracts of the histories of seventeen cases, chiefly in private practice, and described the infarcts in considerable detail. He believed that arterial disease was the primary cause of the infarcts, showed that chronic myocarditis was not a correct term, and asserted that angina pectoris and related symptoms, previously considered purely nervous, had an anatomic basis. Attacks came on after physical or emotional strain, once after attending a new Wagner opera. Besides stenocardia, asthma was sometimes present. Physical signs were rarely described, but irregular heart beat and pulse were noted, and sometimes sudden dizziness or temporary syncope on effort. Collapse, general coolness of the body, weakness and other symptoms were mentioned at times. Huber asserted that the cases represented an important and by no means rare sort of heart failure, centering around disease of the coronary arteries, the latter a part of general arteriosclerosis. Syphilis was present in some cases. Ziegler commented on Huber's article in a later number of *Virchows Archiv* and asserted that the conditions were better known than Huber thought and that he, Ziegler, had often demonstrated the relations to his classes. He agreed with Huber anatomically and clinically.

John Lindsay Steven, clinician and pathologist, who had worked with Huber and Weigert in 1882, gave a

V 19

series of lectures in 1887 on "Fibroid Degeneration and Allied Lesions of the Heart, and their Association with Disease of the Coronary Arteries." A critical examination of the British literature on the topics named showed that in many reports the coronary arteries were not mentioned. Among important conclusions, based on sixteen cases in his own experience, Steven said "The influence of a morbid state of the coronary arteries must be taken into account in considering all diseases of the heart, but especially of the myocardium, and no examination of the heart can be regarded as complete which does not include a careful investigation of the state of those vessels." Also "The possibility of diagnosing fibroid disease and infarction of the heart should always be kept in sight and, by carefully passing in review the whole symptomatology and pathology of a given case of cardiac disease, a correct opinion in this regard may probably be arrived at."

In 1894 Steven reported twenty-one new cases out of 810 consecutive autopsies. In only three cases could the coronary arteries be said to be practically healthy. He concluded that the development of fibroid patches in the heart wall afforded the structural basis of a large number of cases of angina pectoris.

The work of more than a hundred years, of which I have tried to give a fleeting glance, was so diversified in method and conclusions that for a long time no progress seems to have been made. But by 1884 Professor Ernst Leyden, director of the First Medical Clinic in Berlin, was able to decipher a fairly complete picture, which he presented under the title "Ueber die Sclerose der Coronararterien und die davon abhaengigen Krankheitszustaende," in seventy pages of the *Zeitschrift für klinische Medicin* (vol. 7, pp. 458-486, 539-580). He clearly traced the course of discovery in anatomy and clinical features and showed how the early picture of angina faded while disease of the coronary arteries was not susceptible of clinical recognition and theories of neurosis sprang up. For a time angina was rarely mentioned in works on heart disease, and case reports were to be found under such titles as "cardiac apoplexy," "dilatation," "fatty heart" or "weakened heart." Then, while physiologists and pathologists were gathering observations, clinicians slowly added positive knowledge, with Leyden and his associates, and many others, especially in France and Germany, taking part in proving the relations of angina pectoris and coronary arteriosclerosis. From a picture of current clinical opinion he drew the conclusion that greater knowledge of cardiac physiology was needed, including more accurate study of functional phenomena.

Leyden gave many references to contributions of French clinicians, especially Huchard and his school, and prepared the medical world for Huchard's work on Diseases of the Heart and Great Vessels, which appeared in 1889. As it is still used by students of the subject, it is not necessary to speak in detail, but I may point out that fifty years ago Huchard taught that true angina pectoris has as its anatomic cause arteriosclerotic narrowing or obliteration of the coronary arteries, resulting in ischemia of the heart muscle. He made an extensive study of all symptoms then known. With regard to the often troublesome gastric features, he advised that they be treated as angina pectoris, advice still much needed in home care and on the golf course. His discussion of the objections to the coronary theory is still suggestive.

It may well be asked, If the pathogenic relations of the coronary arteries were so well understood fifty years ago, why was not coronary disease more frequently recognized from then on and more accurately treated? One reason, I think, is that the facts were not quickly and widely diffused, and a reason for that is that many other novelties were presented to the medical world at the same time. To name only a few, we had in rapid succession, but also with long and tedious discussions, the causes of sepsis, tuberculosis, typhoid, diphtheria, malaria, pneumonia and meningitis; the development of antisepsis and asepsis; the growth of borderline medicine and surgery; endocrine diseases; peptic ulcer, and appendicitis. What a contrast there was between the way we applied the facts of appendicitis, searching for patients with the condition in an early form and sending them to the operating room for autopsy in vivo, and those of cardiac infarction, handled symptomatically as it had been for a hundred years. At the same time we were working out the slow but rich development of the anatomy and physiology of the heart and the exact study of pharmacology and therapeutics, not yet ended.

OSLER'S POINT OF VIEW

It is interesting to see the attitude of a great contemporary, Dr. Osler, whose conception of coronary disease is sometimes referred to as deficient. When I began to work with him in 1887, after being with Virchow, Huber, Weigert, Leyden and others of the same period, I found him familiar not only with the early history of angina pectoris but with the newer and current papers on coronary disease in English, French and German, receiving the leading periodicals, and using the well stocked periodical room of the College of Physicians. We read and discussed Steven's lectures as they appeared in the *Lancet*. In the laboratory in the University Hospital that Dr. Osler and Dr. John Musser had installed, Dr. Osler had a small collection of hearts with diseased coronaries, including the one from the imbecile in Elwyn Institution, often referred to in lectures and books. In his autopsies he never failed to examine the main trunks and many branches of the coronary arteries. Besides obviously fibroid areas in the heart muscle, he always took cross sections of the papillary muscle in order to search for microscopic foci, with reference to coronary sclerosis.

In the first (1892) edition of the "Practice," the section on Affections of the Myocardium begins: "A knowledge of the changes produced in the myocardium by disease of the coronary vessels gives a key to the understanding of many problems in cardiac pathology." He described anemic infarcts briefly but clearly, also fibrous myocarditis. He said that the symptoms of myocardial disease were notoriously uncertain and that angina was sometimes present in cases of fibroid heart. Angina pectoris was considered under cardiac neuroses, not as an independent disorder but as a symptom associated with a number of morbid conditions of the heart and vessels, more particularly with sclerosis of roots of the aorta and changes in the coronary arteries. He held that true angina was a rare disease and discussed some views as to its nature, such as neuralgia of the cardiac nerves, cramp of the heart muscle and tension of the ventricular walls. He thought Cohnheim's experiments did not throw much light on the etiology of angina pectoris. Pseudo-anginas he considered hysterical and when in doubt advised treating such cases

113
939

as true angina. He included angina among possible results of coronary disease. I still think these articles good textbook material, in advance of the times.

In the editions that followed he made frequent revisions. In the second (1895) edition he added, under myocardial disease, Allen Burns's theory, revived by Potain and others, of ischemia of the heart muscle, and intermittent claudication, and admitted tobacco angina as a rare but well recognized form of disease.

In the third edition (1898) he described the work of F. H. Pratt and added a paragraph on fragmentation and segmentation and modified considerably the section on angina. The fourth (1901) and fifth (1904) editions were not changed. In the sixth (1905) edition typographic alterations were made. Dilatation and hypertrophy were put in the section on diseases of the myocardium, and the text of that section was modified. The most marked change under angina was to replace pseudo-angina by "functional angina pectoris," but Huchard's table of differential diagnosis was retained. The seventh (1909) edition shows no change in myocardial disease or angina pectoris.

In 1897 he published "Lectures on Angina Pectoris and Allied States" and in it began the chapter on "Theories of the Disease" with the coronary artery. In the Lumleian Lectures (1910) he again abandoned pseudo-angina. In chapter II he said "We are all united in the acceptance of the Jennerian view of the close connexion of lesions of the coronary arteries with the disease."

Having early accepted the coronary theory of angina, I sometimes thought Dr. Osler was not as enthusiastic about that as could be wished, but as I talked with him or read his productions I had a feeling that his position was a better one and that he was constantly seeking more light on all the details of the problem. I think that severe angina and infarction were less frequent say up to 1910 than now, certainly in hospitals. The difference of opinion of Osler and Allbutt as to frequency are difficult to explain, but similar differences can be found all through the history of the disease.

SYMPTOMATOLOGY AND PLAN OF TREATMENT

Even in 1910 the data for a diagnosis of coronary disease were not as complete as they were ten years later, and those who ventured a diagnosis of infarct were often in doubt, especially if the patient survived the attack or if, in case of death, there was no autopsy. Pericarditis as a helpful sign was rare or was rarely noted. The use of blood pressure observations was an early addition of some value, also the more accurate recognition of circulatory collapse, but it was not until Libman showed the great importance of leukocyte changes that we had a definite guide. Soon after, Fred Smith showed the value of electrocardiograms, and studies of the sedimentation rate furnished another gain. All these discoveries met Leyden's plea for better knowledge of symptomatology in anginal disease, and no one would have appreciated them more than Osler. He too would have welcomed the more recent studies on pain, including that in diaphragmatic hernia and on chemical changes in heart failure, but at the present time I think he would still show a desire for more light.

There is a wish for a better name than angina pectoris, but until we have more exact knowledge of the minute processes I see no reason for change. But whenever used it must be with the conviction that the name refers only to symptoms and demands a prompt and thorough differential diagnosis to exclude all other causes of pain, or to assign them their significance. Its adoption also necessitates an exact and persistent search for evidences of coronary disease and a prompt and intensive plan of treatment to meet all possibilities. Angina pectoris cannot be given as a cause of death. Thanks to writers and speakers on the subject from the beginning of Herrick's work, there is a very notable ability on the part of the medical profession to recognize and care for coronary patients. I am not in favor of publicity that would cause needless alarm or lead to diagnosis by laymen, but from time to time one can see patients for whom a deeper search, as by an electrocardiogram, would be useful, and for sound advice in examinations of the apparently healthy and to all who seek information on their cardiac problems. In angina patients, and for those who have survived an infarction, we can often improve the outlook for the future by directing activity in ways to favor collateral circulation in the coronary system. Many cases, some of them extremely severe, show that a remarkable degree of recovery is sometimes attained without particular effort. There would probably be more if definite measures were always taken as to exercise and rest, diet and mode of life, and probably by medication based on investigations already made and still to be made.

94 North Madison Avenue.

THE "DEFUNCTIONALIZING" COLOSTOMY (DEVINE)

A RATIONAL PREPARATORY PROCEDURE FOR RESECTION OF LESIONS OF THE LARGE BOWEL

ALTON OCHSNER, M.D.
MICHAEL DEBAKEY, M.D.
AND
JOSEPH ROTHSCHILD, M.D.
NEW ORLEANS

Fatalities following resections of the gastrointestinal tract are due primarily to peritonitis. Because the number and virulence of micro-organisms progress commensurably with the aboral distance from the cardia, peritonitis and mortality following operations on the gastrointestinal tract similarly increase. Shambaugh [1] observed in autopsy series that the incidence of peritonitis was 15.3 per cent in thirty-nine cases in which operations had been performed on the stomach and small bowel, whereas in a group of fifty-two cases in which operations were performed on the large bowel, peritonitis was present in 33 per cent. Although there are other factors influencing the mortality in gastrointestinal resections, the most important is obstruction, because of the consequent increased number and virulence of bacteria in the bowel and the decrease in the local and systemic resistance. Grey Turner [2] reported a mortality rate of 25.7 per cent in seventy one stage resections of the large bowel as contrasted with a mortality of 12.5 per cent in seventy-two multiple stage resections. Cheever [3] showed that the relief of obstruction by means of a preliminary colostomy decreased the mortality rate from 24 per cent in fifty cases without

From the Department of Surgery, Tulane University School of Medicine.

1. Shambaugh, Philip: Peritonitis as a Factor in the Mortality of Gastrointestinal Surgery, Ann. Surg. 104: 382 (Sept.) 1936.
2. Turner, G. G.: Cancer of the Colon, Lancet 1: 1017 (May 18) 1929.
3. Cheever, David: The Choice of Operation in Carcinoma of the Colon, Ann. Surg. 94: 705 (Oct.) 1931.

colostomy to 8.5 per cent in thirty-five cases with preceding decompression. Almost identical results were obtained by von Haberer,[4] who reported 25 per cent fatalities in 172 cases without colostomy and 8 per cent fatalities in 109 cases with colostomy. Arthur Allen [5] reports from the Massachusetts General Hospital a 6 per cent incidence of peritonitis in 400 cases of one stage resection of the large bowel and a 3.5 per cent incidence in 253 two stage resections of the colon. As demonstrated by these figures, the mortality rate has been reduced materially by the institution of preoperative measures. Generally, these have consisted of relief of obstruction only, without special attempts to decrease the bacterial flora of the involved segment. The procedures usually employed have been enterostomy, cecostomy, appendicostomy and lateral and double-barrel colostomy. On the other hand, operations on obstructed large bowel still are attended with considerable risk, because of the danger of peritonitis as well as the interference with healing of the bowel wall which the usually employed decompressive procedures affect relatively little, because they do not decrease the number of pathogenic micro-organisms.

As long as fecal contamination of a bowel segment occurs, there will be little decrease in the pathogenicity of the micro-organisms within the intestine. Whereas a double-barrel colostomy deviates a great part of the fecal stream, almost invariably some soiling of the distal segment occurs. Only by entirely excluding a segment of the bowel from fecal contamination can there be any material diminution in the bacterial content of the bowel. The complete isolation of the openings in the proximal and distal segments will prevent the entrance of feces into the distal portion.

Whereas the separation of the proximal and distal openings in the performance of a permanent colostomy was suggested by Mixter,[6] credit for first emphasizing the importance of isolation of the two bowel openings as a preliminary decompressive and preparatory procedure belongs to Sir Hugh Devine [7] of Melbourne, Australia.

The rationale of the Devine type of colostomy is dependent on the complete "defunctionalization" of the bowel distal to the colostomy. By completely deviating the fecal stream away from an involved portion of the bowel, there is obtained relief of obstruction and, equally or even more important, absence of fecal contamination, which results in marked diminution and even virtual disappearance of the micro-organisms. Devine has termed this "debacterialization." As emphasized by Devine, the safety of resection of a lesion of bowel under such circumstances is assured not only because of the decreased number or absence of pathogenic bacteria at the anastomotic site but also because of the normal blood supply and intestinal tone, both of which are necessary for optimal healing. It is the common experience of surgeons that healing of intestinal wounds is poor in those instances in which there is lowering of the local resistance of the bowel as a result of stasis, diminished blood supply, inflammatory reaction in the bowel and decrease in intestinal tone. Whereas healing of intestinal wounds usually occurs promptly under ordinary conditions even though the normal pathogenic organisms are present in the bowel, much better healing can be secured following the use of the Devine colostomy because of the "debacterialization" of the involved segment. "Debacterialization" and "defunctionalization" of the involved segment not only favor optimal healing of an intestinal anastomosis but also, because of the increased operability which results following the complete subsidence of an inflammatory process, make possible resections which otherwise could not be done. Not infrequently a mass, which on preliminary examination at the time of the performance of the colostomy appears to be inoperable because of its size and fixation, at subsequent exploration is found to be not only operable but also relatively easily resectable. As a result of complete "defunctionalization" of the colon there occurs, in addition to the local improvement in the lesion, general improvement in the patient. This is particularly true in patients with

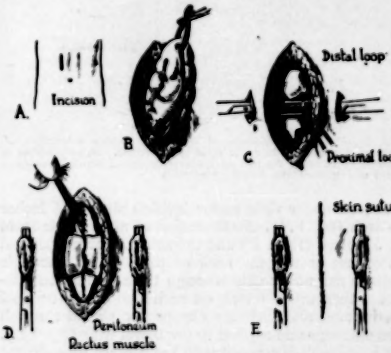

Fig. 1.—Technic of colostomy originally devised by Devine: *A*, upper right rectus skin incision about 2½ inches in length. *B*, formation of long spur (from 4 to 5 inches) by approximating opposed surfaces of proximal and distal limbs of loop of transverse colon. *C*, through buttonhole openings, made 1 inch on each side of original skin incision and extending through subcutaneous tissue only, Ochsner clamps are passed and applied to bowel wall, which is severed with the cautery between the clamps. *D*, cut ends of bowel are drawn into the buttonhole openings by the forceps and wound closed around neck of loop. *E*, original skin incision is closed.

inflammatory lesions. We believe also that following the use of the Devine colostomy it is possible to perform much more extensive resections than would be considered otherwise, because the safety of an operation of such magnitude is much greater in an individual who has been well prepared and whose bowel is in an optimal condition.

"Debacterialization" of the involved segment can be hastened by mechanically flushing out the segment by the introduction of fluids—either saline solution or, as suggested by Devine, antiseptics—into the distal colostomy opening and allowing them to pass through the involved bowel. Occasionally, irrigation through the distal segment is not possible because of complete obstruction. In such instances we have found that the introduction of pure cultures of Bacillus acidophilus in the involved segment both proximal and distal to the obstructing lesion will quickly free the segment of pathogenic bacteria. It is extremely important to employ

4. von Haberer, Hans: Erfahrungen mit der einzeitigen Dickdarmresektion und Verbesserung ihrer Technik, Wien. klin. Wchnschr. **50**: 825 (May 28) 1937.

5. Allen, Arthur W.: Right Colectomy for Malignant Disease: A Discussion of the Mortality Associated with Various Operative Procedures, J. A. M. A. **109**: 923 (Sept. 18) 1937.

6. Mixter, S. J.: Unpublished technic cited by Gould, Alfred H.: The Technic of Operations upon the Intestines and Stomach, Philadelphia, W. B. Saunders Company, 1906.

7. Devine, H. B.: Carcinoma of the Colon, Brit. M. J. **2**: 1245 (Dec. 28) 1935; Excision of the Rectum, Brit. J. Surg. **25**: 351 (Oct.) 1937; Operation on a Defunctioned Distal Colon, Surgery **3**: 165 (Feb.) 1938.

fresh active cultures of B. acidophilus, as the usual commercial preparations are ineffective. It is also important to use large quantities of the cultures, because if employed in insufficient amounts they are valueless.

TECHNIC

The procedure as originally described by Devine has been modified by us in an attempt to simplify the technic and diminish the possibility of wound contamination. The operation described by Devine consists of

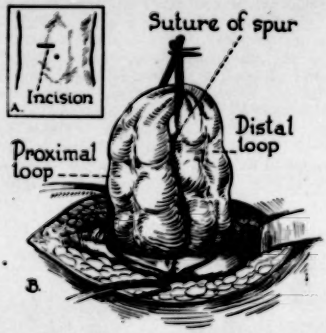

Fig. 2.—Authors' modification of technic of Devine colostomy: *A*, transverse skin incision in upper right rectus region. *B*, stabilization of two limbs of colon by traction on rubber tube passed through mesentery at apex of loop facilitates formation of spur.

making an upper right rectus incision about 2½ inches in length (fig. 1 *A*), the formation of a long spur from 4 to 5 inches, (fig. 1 *B*) and the suturing of the parietal peritoneum around the neck of the loop. Buttonhole openings extending only through the subcutaneous tissue are then made 1 inch on each side of the original skin incision and Ochsner clamps are passed through these openings and applied to the bowel wall (fig. 1 *C*). The bowel wall is severed with the cautery between the clamps, and the cut ends are drawn into the buttonhole openings by the forceps (fig. 1 *D*). The original skin incision is then closed (fig. 1 *E*).

The obvious disadvantage of this procedure is the possibility of contamination from the cut ends of the bowel as they are drawn through the subcutaneous tissue into the buttonhole openings on either side of the original incision. In spite of cauterization of the severed ends of the bowel, asepsis cannot be absolutely assured. That this is an actual as well as a theoretical danger is demonstrated by the occurrence of wound infections in the first few cases in which this procedure was performed by us. Moreover, the applied Ochsner clamps (the distal one of which must remain in position for about one week postoperatively) are bulky, are awkward and limit the patient's movements. By slightly modifying the procedure we have overcome these disadvantages.

The skin incision is made transversely (about 8 to 9 cm. in length) instead of longitudinally (fig. 2 *A*). The purpose of making the skin incision transversely instead of longitudinally is to obviate the necessity of subsequently making separate buttonhole incisions for the proximal and distal ends of the bowel. Moreover, as the severed ends of the bowel may be placed at the respective ends of the skin incision which may be sutured between the bowel openings, the possibility of wound contamination is avoided. The upper and lower flaps are mobilized slightly and retracted longitudinally. The incision in the rectus sheath is made longitudinally through its mid portion and the rectus muscle split. The peritoneal cavity is opened by incising the posterior rectus sheath and peritoneum longitudinally. Through this small incision a preliminary exploration may be accomplished readily by lubricating the gloved hand with sterile petrolatum or liquid petrolatum, as originally advocated by Devine. This simple procedure greatly facilitates introduction of the hand into the peritoneal cavity through such a small incision. The presence of metastatic involvement as well as probable operability of the neoplasm may be determined by this preliminary examination.

The next step in the operation is the formation of the colostomy. A loop of transverse colon is delivered into the wound, and the mesentery of the apex of the loop is ligated and divided for a distance of about 2 cm. A soft rubber tube is passed through this opening in the mesentery at the apex of the loop and traction on the tube stabilizes the two limbs of the colon (fig. 2 *B*). The two opposing surfaces of the bowel segments are approximated for a distance of about 10 cm. by a continuous suture of chromic 0 catgut, thus forming a spur (fig. 2 *B*). If difficulty is encountered in performing this because of a short transverse colon, the hepatic flexure may be mobilized and the ascending and transverse colon used to form the spur. Once the spur is formed, the connected limbs of the bowel are pushed back into the peritoneal cavity and the peritoneum and anterior rectus sheath are sutured around the neck of the loop.

At this stage, clamps are applied to the bowel. Ochsner clamps may be used and are applied transversely to the loop of the bowel with the handles directed caudally. Before applying the clamps we strip the bowel in order to empty the loop and decrease its diameter, thus facilitating puckering of the bowel at the site of application of the clamps. As emphasized by Devine, the openings in the bowel and also in the skin should be small to

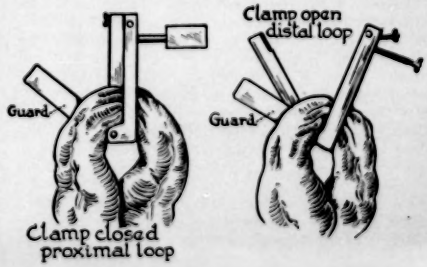

Fig. 3.—Application of proximal and distal clamps to bowel wall in vertical manner. It should be observed that the bowel is puckered and applied as close to the hinged end of the clamp as possible. This facilitates the subsequent placing of the skin suture close to the bowel.

favor better control of fecal evacuation. The bowel is severed between the proximal and distal clamps by means of the cautery and placed in the respective ends of the skin incision, which is sutured between the two ends of the bowel. However, a special clamp has been devised which obviates the previously mentioned disadvantages of the forceps. This special instrument consists of two clamps, which may be held rigidly apart

at the required distance by means of an attachable horizontal bar. Each clamp consists of two jaws hinged at one end with a swivel thumb screw at the other end for bringing the jaws together with a crushing force. The crushing surfaces of the blades are serrated to prevent slippage of the crushed bowel wall. A metal blade the width of the clamp is hinged at one end on the upper surface of the two jaws. After the clamps have been applied and the bowel wall severed this metal blade is turned on its hinge, as the blade of a knife, to cover

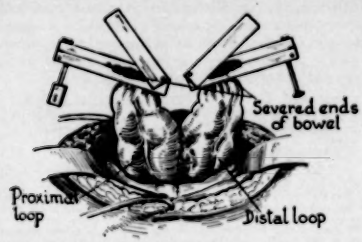

Fig. 4.—Bowel wall severed with cautery between proximal and distal clamps and guards folded in position over severed ends of bowel, thus preventing completely the possibility of contamination during subsequent manipulation.

entirely the severed end of the bowel, and thus acts as a guard to prevent the possibility of contamination. To each clamp there is attached at right angles a side piece, which may be applied to a horizontal bar for the purpose of stabilizing and holding the clamps apart at the desired distance, thus obviating the tension on the suture line and the possibility of its being torn during manipulation.

In operation this instrument greatly facilitates the procedure. The proximal and distal clamps are applied to the bowel wall as illustrated in figure 3. When the clamp is applied, the bowel is puckered similarly as described and placed as close to the hinged ends of the clamp as possible. This facilitates the placing of the skin suture close to the bowel. It should be observed also that the clamps are applied in a vertical rather than a horizontal manner. This prevents subsequent rotation of the bowel as the respective openings are placed in position at each end of the skin incision. The bowel is severed with the cautery between the clamps, and the guards are folded in position over the severed ends of the bowel (fig. 4). The two clamps with the crushed bowel ends are now separated in a fanlike manner to lie transversely, the respective segments of the bowel being placed in the extreme ends of the incision. The separation of the bowel segments in these positions permits closure of the skin incision except for buttonhole openings at either end through which the puckered bowel ends protrude. The horizontal bar is applied to each side piece of the clamp. One end of the bar is attached rigidly to the side piece of one clamp by means of a square joint, whereas the other end is fastened by a sliding joint, which may be tightened once the two clamps are separated the required distance (fig. 5). The wound is then closed by suturing each end of the anterior rectus sheath around the neck of the approximated limbs of bowel (fig. 5). The edges of the skin incision between the proximal and distal ends of the bowel are finally approximated (fig. 6). Twenty-four hours later the proximal clamp as well as the horizontal bar and the side piece of the distal clamp are removed because the two segments of bowel are fixed to each other by the "spur" suture. Only the distal clamp is necessary (fig. 7) for the purpose of maintaining proper position of the bowel ends and preventing their retraction until they become adherent to the abdominal wall. The distal clamp is not removed for one week or ten days because this period of time is required for adequate fixation of the bowel to the parietes. Immediately following removal of the distal clamp, irrigation of the involved segment can be instituted in order to cleanse the segment and hasten its debacterialization.

As suggested by Devine, occasionally it may be necessary in cases with complete obstruction and with considerable distention that a preliminary cecostomy be done as a decompressive procedure before the performance of a "defunctionalizing" colostomy. This was satisfactorily done in one of our cases. After cleansing and debacterialization has been accomplished, which requires from ten days to three weeks, resection of the involved segment can be performed safely because of absence of infection and because of normal blood supply and tone of the bowel.

In nonmalignant lesions in which resection of the involved segment is not urgent, it is desirable to allow a long period of time to elapse before extirpation of the bowel in order to permit the inflammatory process to subside completely. This is particularly true in cases of diverticulitis in which because of stagnation of fecal contents in the diverticula infection may persist even months after the colostomy. This is clearly illustrated by one of our patients with localized diverticulitis and cicatrical narrowing of the sigmoid, who had several exacerbations of sigmoiditis weeks following complete "defunctionalization" of the distal bowel. The resection is usually done through an incision in the lower left quadrant of the abdomen. Because of the "defunctionalization" and debacterialization with almost complete subsidence of all inflammation, extirpation of the involved segment and its regional lymphatics is possible.

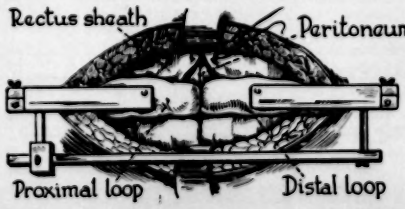

Fig. 5.—The two ends of the bowel have been separated the desired distance and stabilized in this position while the wound is being closed, thus obviating tension on the suture line and possibility of its being torn during manipulation.

Reestablishment of continuity of the bowel is done by an end to end anastomosis with little or no danger of insufficiency of the suture line because of the optimal conditions under which the bowel is permitted to heal. There is no urgency in redirecting the fecal stream through the involved segment following resection. This is illustrated in one of our cases in which ten days after the performance of the anastomosis a barium sulfate enema showed a small defect at the line of anastomosis without any clinical manifestations of insufficiency of

the suture line. Two weeks later the defect had completely disappeared and the fecal stream was redirected through the distal segment. In this particular case had there not been complete "defunctionalization" of the colon there probably would have resulted at least a localized peritonitis. The complete debacterialization and "defunctionalization" permit the performance of not only more radical procedures, as mentioned, but also resection of lesions located just above the pelvic floor and reestablishment of continuity of the bowel by end to end suture. In many cases with low sigmoidal lesions, abdominoperineal resections can thus be obviated. In one of our cases the condition of the lesion in the lower sigmoid at the time of exploration during the performance of the colostomy indicated its inoperability. It was hoped, however, that "defunctionalization" and debacterialization would result in sufficient decrease in size and fixation to make excision possible. At the second operation it was found that whereas the growth had decreased somewhat in size it was still fixed posteriorly and extended well into the rectum, obviating resection and reestablishment of continuity of the bowel. An abdominoperineal resection of the rectum and sigmoid was decided on and during the freeing of the rectum from the left wall of the pelvis the rectum tore, causing spillage and contamination of the peritoneum. The material was immediately removed and although a possible peritonitis from this contamination was anticipated the postoperative course was exceptionally smooth, there being only a slight febrile reaction. Undoubtedly the reason the patient did not develop a peritonitis as a result of contamination was the relative debacterialization produced by the "defunctionalizing" colostomy. Had we known that the size of this lesion would not have subsided sufficiently to permit excision and reestablishment of continuity of the bowel, it probably would have been better in this particular case to perform a two stage abdominoperineal resection as suggested by Lahey.[8]

In the performance of the abdominoperineal resection the special clamps for use in our modification of the Devine colostomy can also be applied for the ends of

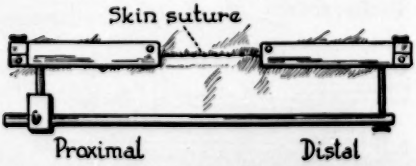

Fig. 6.—The edges of the skin incision between the proximal and distal ends of the bowel are sutured, thus completing the operation.

the divided sigmoid. Thus, once the clamps are applied and the bowel severed with the cautery between them, the guards are folded over the severed ends of the bowel, permitting handling of the bowel with absolute assurance of asepsis.

Before redirecting the fecal stream through the distal segment, one should determine patency and sufficiency of the anastomosis by barium enema and x-ray examination. Generally a minimum of two weeks should elapse before diversion of the fecal stream.

8. Lahey, F. H.: Two Stage Abdominoperineal Removal of Cancer of the Rectum, Surg., Gynec. & Obst. 51: 692 (Nov.) 1930. Lahey, F. H., and Cattell, R. B.: Two Stage Abdominoperineal Resection of the Rectum and Rectosigmoid for Carcinoma, Am. J. Surg. 27: 201 (Feb.) 1935.

The reestablishment of the function of the distal colon is accomplished by crushing the spur between the proximal and distal limbs of the colostomy, by means of a specially devised enterotome which permits destruction of the opposing bowel walls without crushing the intervening skin between the colostomy openings. Whereas this may be done by the clamp devised for this purpose by Devine, it has been found to have certain disadvantages. It is bulky and inconvenient because of its weight and long handles which project above the skin surface. In an attempt to overcome these objections we have devised a special clamp which possesses lightness in weight, simplicity in design, facility in appli-

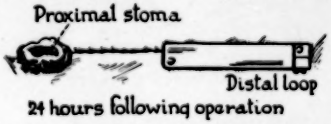

Fig. 7.—Twenty-four hours postoperatively the proximal clamp as well as the horizontal bar and the side piece of the distal clamp are removed. Because the two limbs of the bowel are held together by the spur suture, only the distal clamp is necessary for the purpose of maintaining proper position of the bowel ends and preventing their retraction until they become adherent to the bowel wall.

cation and convenience in operation. This enterotome, which has been described previously,[9] consists of only two working parts (fig. 8) and is constructed of duraluminum to give lightness in weight. Its application is extremely simple and consists merely of introducing the blades into the respective colostomy openings and fitting the crossbars and screw of one arm of the clamp in their corresponding openings in the other arm (fig. 9). By turning the screw wheel, one causes the crushing blades to approximate each other. Its lightness in weight and the fact that the handles project only about 3 cm. above the skin surface make it extremely convenient. An ordinary dressing may be applied and the patient may walk about during the several days required for the blades to cut through the spur.

We have used this procedure in twenty-six cases, in ten of which malignant lesions of the bowel involved the sigmoid or rectosigmoid, and in sixteen the lesions were nonmalignant. Of the latter sixteen cases there was one of diffuse ulcerative colitis in which an enterostomy of the Devine type was performed in the terminal ileum. There were two cases of sigmoidal diverticulitis with cicatricial narrowing of the bowel. One was a sigmoiditis unassociated with diverticulitis. There were two sigmoid fecal fistulas, both of which followed hysterectomy done elsewhere. One of these was associated with a tuberculous endometritis. In this instance the tuberculous infection may have been responsible for the persistence of the fecal fistula. In the other case because of extensive injury to the sigmoid at the time of hysterectomy a colostomy was performed in the upper sigmoid with blind closure of the distal rectosigmoid. In the remaining ten of the nonmalignant group there were rectal strictures produced by venereal lymphogranuloma.

In eleven of the sixteen cases of nonmalignant diseases, only the preparatory "defunctionalizing" colostomy has been done. As mentioned before, long periods of time are allowed to elapse before resections in inflammatory lesions. In eight of these eleven are rectal

9. DeBakey, Michael, and Ochsner, Alton: A New Clamp for the Devine Colostomy, Surgery 5: 947, 1939.

strictures due to venereal lymphogranuloma, and in one is an associated rectovaginal fistula. In two there are diverticulitis and cicatricial stenosis of the sigmoid. Trauma to the sigmoid occurred in one during hysterectomy for tuberculous endometritis. In five of the cases of nonmalignant lesions resections of the disease processes have been done. The patient with ulcerative colitis has had a total colectomy with a permanent enterostomy. Two had resections of the rectal stricture produced by venereal lymphogranuloma. One had a localized sigmoiditis with cicatricial narrowing without diverticulitis. One who had had a previous resection of a considerable portion of the sigmoid and blind closure of the rectosigmoid stump because of operative injury to the sigmoid during performance of hysterectomy has had successful implantation of the sigmoidal loop into the blind rectal segment beneath the peritoneal floor. All of these except the patient who had total colectomy for ulcerative colitis had reestablishment of continuity of the bowel.

Of the ten cases in which there were malignant lesions the tumor was located in the sigmoid or rectosigmoid in all but one, in which it was situated in the splenic flexure. In six of these ten cases, resections of the involved segment had been done. Three were found to be inoperable at the second operation so that the "defunctionalizing" colostomy was left as a permanent one and there was one death following the colostomy. Of the six cases in which extirpation of the malignant lesion was accomplished there was return of normal

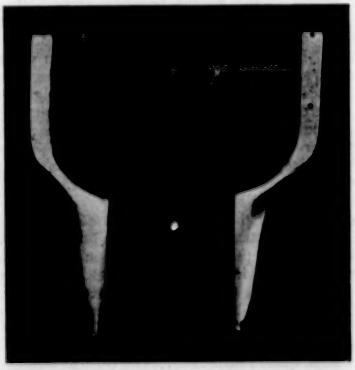

Fig. 8.—Authors' enterotome for crushing the spur between the proximal and distal limbs of the colostomy to reestablish function of the distal colon. The instrument, which is constructed of duraluminum to give lightness in weight, consists of two arms, the upper part of which serve as handles and the lower part as crushing blades. Two right-angle cross bars are rigidly attached to the handle of one arm of the clamp and corresponding openings are present in the other arm of the clamp, through which these cross bars slide. The screw-bar provided with a wheel is also firmly attached to one arm of the clamp, with a corresponding screw opening in the other arm of the clamp.

bowel function except in two cases in which the lesion in the rectum obviated reestablishment of bowel continuity.

Of the total series of twenty-six cases only the "defunctionalizing" colostomy was done in eleven, in all of which there were inflammatory lesions. Of the eleven patients who had the second stage completed, all recovered. Six were for malignant lesions and five were for nonmalignant lesions. Three patients with malignant lesions had subsequent explorations but the lesion was found to be inoperable so that the defunctionalizing colostomy was left as a permanent one. One patient with a malignant lesion died following the performance of the colostomy.

This fatality was apparently the result of overzealous postoperative therapy:

A Negro aged 56 was admitted to Charity Hospital with a history of acute intestinal obstruction of four days' duration. His abdomen was markedly distended and in the left lower quadrant a large palpable mass was present. X-ray examination following a barium sulfate enema showed complete obstruction in the sigmoid. Following twelve hours' preoperative preparation with Wangensteen duodenal suction, a Devine colostomy of the transverse colon was performed. There was considerable edema of the mesentery and distention of the bowel which made the operation difficult. The clamp on the proximal limb was removed after twenty-four hours and the immediate postoperative convalescence was satisfactory in that the postoperative febrile reaction returned to almost normal within four days. There was, however, retraction of the medial portion of the proximal opening probably resulting from the subsidence of the edema. There was also considerable relief in abdominal distention. Because on the sixth postoperative day the attending surgeon thought there was insufficient evacuation from the proximal opening in spite of diminished distention, an attempt was made to introduce a catheter into the proximal opening, which because of the retraction of the medial portion of the proximal opening resulted in a false passage of the catheter into the peritoneal cavity. Shortly thereafter the patient suddenly went into shock and exhibited manifestations of peritonitis. Death followed in twenty hours. Unfortunately an autopsy was not obtained but apparently death was a result of massive intraperitoneal contamination. It is our opinion that this could have been obviated had there been no postoperative manipulation of the wound. It is possible that it would have been better because of the complete obstruction and marked distention to have performed a preliminary cecostomy as suggested by Devine. The subsidence of the distention and edema of the bowel was probably responsible for retraction of the medial part of the proximal opening.

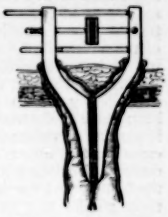

Fig. 9. — Diagrammatic illustration of assembled enterotome in position in the colostomy.

SUMMARY

The technic of the "defunctionalizing" colostomy originally described by Devine has been modified. The performance of the colostomy is greatly facilitated by a specially devised clamp.

This procedure was employed in twenty-six cases. There were malignant lesions of the bowel in ten of this group involving the sigmoid or rectosigmoid, and nonmalignant lesions in sixteen.

In six of the ten cases in which there were malignant lesions resection of the involved segment resulted in return of normal bowel function except in two cases, in which the lesion in the rectum obviated reestablishment of bowel continuity.

Resections of the disease processes in five of the sixteen cases in which there were nonmalignant lesions resulted in return of normal bowel function except in one, in which a total colectomy was done.

There was only one death in the total series and this followed the colostomy and probably was preventable.

1430 Tulane Avenue.

THE HEART IN ANTHRACOSILICOSIS

JOHN F. GIERING, M.D.
WILKES-BARRE, PA.
AND
ROBERT CHARR, M.D.
PHILADELPHIA

Congestive heart failure is a common occurrence in cases of far advanced anthracosilicosis. In a series of postmortem examinations made on anthracite miners,[1] heart disease was found to be twice as common in the miners as in nonminers. At the White Haven Sanatorium it was noted that the most common symptom of the anthracite miners was dyspnea of varying severity, and it was difficult at the time of admission to determine whether this dyspnea was due to cardiac insufficiency or to anthracosilicosis. Attempts have been made to determine whether dyspnea in such cases is cardiac or pulmonary in origin by studying the vital capacity, the venous pressure and the velocity of pulmonary circulation in addition to considering carefully the history and the physical evidence.[2] It was noted in these studies that an estimation of the pulmonary circulation time was an aid in detecting failure of the right side of the heart. However, this test was found to be inaccurate in several instances, and prolongation of the time was found only in the cases in which definite heart failure was present.

In the present study only the miners without clinical evidences of congestive heart failure were studied. Attempts had been made to detect early pathologic changes in the heart secondary to anthracosilicosis by using the electrocardiographic as well as clinical and laboratory studies.

MATERIAL

Twenty-five miners were studied. Sixteen had anthracosilicosis without complicating pulmonary tuberculosis. Nine had either moderately advanced or far advanced pulmonary tuberculosis in addition to anthracosilicosis. The condition of the heart in these two groups was studied.

METHOD

The past and present medical histories of the miners were carefully investigated with a view to discovering past infection which might have had some influence on the heart. Thorough physical examination of the lungs and heart was made and the presence of any abnormal signs noted. A urinalysis, Mosenthal test, Wassermann test and blood count were made. The venous pressure was determined in every case by the method of Moritz and von Tabora,[3] the vital capacity by the method of Peabody and Wentworth,[4] and the pulmonary circulation and complete circulation times by means of paraldehyde, 0.8 cc. (Candel [5]), and a 20 per cent solution of calcium gluconate, 2 cc. (Baer and Slipakoff [6]). In each case a roentgenogram of the heart was made at a distance of 6 feet. Functional tests were performed, such as counting the pulse rate with normal respiration, after deep inspiration and after a "stepping" test with a view to estimating how well exertion was tolerated. Electrocardiographic studies were made by one of us (J. F. G.), using the three conventional leads and six precordial leads as advocated and recommended by the Committee on Precordial Leads of the American and British Heart Associations. Examinations of the eyegrounds were made with a view to determining the presence or absence of arteriosclerosis.

RESULTS

The ages of the miners varied from 36 to 67. The duration of their occupation varied from three to forty years. All the miners had either moderately or far advanced anthracosilicosis, as evidenced by either nodular or massive consolidation in the lungs revealed by roentgenographic examinations. Eleven, in addition to anthracosilicosis, had either moderately or far advanced pulmonary tuberculosis. The results of urinalysis in all the cases were practically normal. The Mosenthal tests were negative. A Wassermann test of the blood was positive in two cases. The blood counts showed secondary polycythemia in most instances, the number of erythrocytes varying from 5.6 to 6.7 million. In these cases the hemoglobin content as estimated by Sahli's method was more than 100 per cent. Secondary polycythemia was common in association with nontuberculous anthracosilicosis.[7] In cases of anthracosilicosis complicated by very far advanced pulmonary tuberculosis it was infrequently encountered.

The vital capacity was reduced in all cases from 20 to 70 per cent and in direct proportion to the extent of the anthracosilicosis.

Estimation of the venous pressure showed that in most cases it was within the normal limits, which, according to Moritz and von Tabora, are 4 and 10 cm. of water. In only four cases was the venous pressure somewhat above the normal, and even in these cases there was no definite clinical evidence of right-sided heart failure. There was no evidence of edema of the ankles or pulmonary congestion. In eight cases the edge of the liver could be palpated below the right costal margin on deep inspiration. However, in no case was the liver considered to be enlarged secondarily to cardiac decompensation.

The velocity of the pulmonary and of the complete circulation were practically normal in all the cases. For estimation of the pulmonary circulation time, Candel advocated using at least 1.4 cc. of paraldehyde. However, we found that this amount produced dangerously excessive coughing, which in a few instances was followed by extreme shortness of breath. In this study we reduced the amount of paraldehyde to 0.8 cc. and the results were quite satisfactory. The normal pulmonary circulation time, according to Candel, is from 3 to 9.5 seconds. The complete circulation time was determined, 2 cc. of a 20 per cent solution of calcium gluconate being used. Baer and Slipakoff found that the normal complete circulation time varied from nine to sixteen seconds.

Roentgenographic examination of the heart showed no enlargement except in two cases. In these there was an increase in the transverse diameter both to the right and to the left, more marked on the right side. The pulmonary conus was prominent in one case. The aortic knob was prominent in most, with a suggestion of calcification of the aorta in four cases.

The examinations of the eyegrounds showed early or advanced arteriosclerosis in all the cases.

From White Haven Sanatorium, White Haven, Pa., and the Department for Diseases of the Chest, Jefferson Medical College Hospital.

1. Charr, Robert; Cohen, A. C., and Bettag, O. L.: Internat. Clin. **3**: 194-199, 1938.
2. Charr, Robert, and Riddle, Ransford: Am. J. M. Sc. **194**: 502-504, 1938. Charr, Robert, and Savacool, J. W.: Pennsylvania M. J. **42**: 35-38, 1938.
3. Moritz, F., and von Tabora, D.: Deutsches Arch. f. klin. Med. **98**: 475, 1910.
4. Peabody, F. W., and Wentworth, J. A.: Clinical Studies of the Respiration, Arch. Int. Med. **20**: 443 (Sept.) 1917.
5. Candel, S.: Ann. Int. Med. **12**: 236-243, 1938.
6. Baer, S., and Slipakoff, B. G.: Am. Heart J. **16**: 29-43, 1938.
7. Cohen, A. C.: Unpublished data.

The electrocardiographic studies showed the following deviations from the normal in the standard leads:

CASE 1.—*Age 51, moderately advanced anthracosilicosis.* P_1 was inverted. The PR interval was increased. The amplitude of T_1 and T_2 was low. ST_1 took off about 1 mm. above zero level. QRS_1 was of low amplitude. There was slight slurring of QRS_2.

CASE 2.—*Age 48, moderately advanced anthracosilicosis.* P was iso-electric in the three standard leads. T_1 and T_2 were iso-electric. T_3 was of low amplitude. There was slight slurring of QRS.

CASE 3.—*Age 37, moderately advanced anthracosilicosis.* ST_1 was concave. ST_1, ST_2 and ST_3 took off from 1 to 2 mm. above the zero level. Sinus tachycardia was present.

CASE 4.—*Age 45, moderately advanced anthracosilicosis.* A "coronary" type of ST_1 was present. There was slight convexity of ST_2. ST_3 was concave. The three conventional leads, together with the precordial leads, were diagnostic of anterior coronary occlusion. Q_3 measured more than 25 per cent of the largest amplitude of QRS shown in any lead of this record. Sinus tachycardia was present.

CASE 5.—*Age 60, far advanced anthracosilicosis.* QRS_3 and P_3 were of low amplitude. T_3 was iso-electric. ST_1 was concave. There were sinus tachycardia and left axis deviation.

CASE 6.—*Age 59, far advanced anthracosilicosis.* T_3 was of low amplitude. P_3 was iso-electric. Sinus tachycardia and left axis deviation were present.

CASE 7.—*Age 58, far advanced anthracosilicosis.* P_1 was iso-electric. QRS_1 was of low amplitude. There was an occasional auricular extrasystole.

CASE 8.—*Age 51, far advanced anthracosilicosis.* P_2 was abnormally high. P was peaked. There were slurring of QRS and right axis deviation.

CASE 9.—*Age 36, far advanced anthracosilicosis.* There was coarse notching of QRS_3, and QRS_2 was of low amplitude.

CASE 10.—*Age 67, far advanced anthracosilicosis.* P was of low voltage. There was slight slurring of QRS_1 and QRS_2. QRS_3 was of low amplitude, with coarse notching. T_3 was of low amplitude. There was left axis deviation.

CASE 11.—*Age 53, far advanced anthracosilicosis.* P_1 was iso-electric. T_1 and QRS_1 were of low amplitude. QRS_1 was slurred and notched. There was slight slurring of QRS_2 and QRS_3. Lead 1 showed definite abnormalities.

CASE 12.—*Age 58, far advanced anthracosilicosis.* The PR interval was increased. T_1 was of low amplitude. QRS was of low voltage, with coarse notching. There was left axis deviation.

CASE 13.—*Age 61, far advanced anthracosilicosis.* ST_1 was concave upward. It took off 2 mm. above the zero level. ST_2 took off 1 mm. above this level.

CASE 14.—*Age 56, far advanced anthracosilicosis.* P_2 was diphasic. ST took off 2 mm. above zero. There was slurring of QRS. QRS_2 was of low amplitude. Q_3 was notched and measured 16 mm. There was left axis deviation.

CASE 15.—*Age 44, far advanced anthracosilicosis.* P_3 and T_3 were inverted. P_1 and P_2 were peaked. ST_3 was convex upward and took off 1 mm. above zero. There were left axis deviation and sinus tachycardia.

CASE 16.—*Age 51, far advanced anthracosilicosis.* P_1 was of low amplitude. ST_1 was concave and took off 1 mm. above zero. There was slight slurring of QRS_3.

CASE 17.—*Age 50, moderately advanced anthracosilicosis with tuberculosis.* The PR interval was increased. ST_1, ST_2 and ST_3 were concave. The ST intervals in the three standard leads took off from 1 to 2 mm. above the zero level. QRS_1 and QRS_3 were of low amplitude. There was slurring of the down stroke of R_3. P was notched.

CASE 18.—*Age 53, moderately advanced anthracosilicosis with tuberculosis.* P_1, P_2 and P_3 were iso-electric. T_2 and QRS_2 were of low amplitude. QRS_1 was slurred. Sinus tachycardia and right axis deviation were present.

CASE 19.—*Age 62, moderately advanced anthracosilicosis with tuberculosis.* T_3 was of low amplitude. The QRS complex was of low voltage. P_1 was of low amplitude. Left axis deviation was present.

CASE 20.—*Age 42, moderately advanced anthracosilicosis with tuberculosis.* T_1 was iso-electric. T_2 and T_3 were inverted. P_1 and P_2 were peaked. ST_3 was convex. There were slight slurring of QRS_1, QRS_2 and QRS_3, right axis deviation and sinus tachycardia.

CASE 21.—*Age 38, moderately advanced anthracosilicosis with tuberculosis.* P_1 and P_2 were notched. T_3 was of low amplitude. ST_1 was concave upward and took off 1 mm. above zero. ST_2 took off 1 mm. above zero. There were slight slurring of QRS_3, left axis deviation and sinus tachycardia.

CASE 22.—*Age 48, far advanced anthracosilicosis with tuberculosis.* P in all leads was of low voltage. T_3 was iso-electric. QRS in all leads was of low voltage. ST in all leads was concave. ST_1 and ST_2 took off 1 mm. above the zero level. There were sinus tachycardia and left axis deviation.

CASE 23.—*Age 44, far advanced anthracosilicosis with tuberculosis.* T was of low voltage. There were occasional ventricular extrasystoles. Sinus tachycardia was present.

CASE 24.—*Age 42, far advanced anthracosilicosis with tuberculosis.* P_1, P_2 and P_3 were peaked. P_1 and P_2 were higher than the normal figure of 2 mm. as described by Pardee. T was of low voltage. ST_2 took off below the zero level. There were coarse notching of QRS_3, left axis deviation and sinus tachycardia.

CASE 25.—*Age 49, far advanced anthracosilicosis with tuberculosis.* T_3 and P_3 were of low amplitude. QRS was of low amplitude, with marked slurring. Sinus tachycardia was present.

It is of particular interest that of these twenty-five cases of cor pulmonale, in the majority if not all of which one would expect to find right ventricular preponderance (right axis deviation), this occurred in only three cases. On the other hand, left ventricular preponderance (left axis deviation) was present in ten cases. There was no axis deviation in twelve cases. Roentgenograms of the heart revealed no appreciable displacement of the heart in any of the cases. Axis deviation in this series was determined by the triangulation method of Einthoven.

Coronary occlusion was present in one case.

Indications of myocardial or vascular damage were low amplitude of individual waves and low voltage of the various complexes in the three standard leads, and they were present in all except cases 3, 9 and 25. Slurring and notching of the QRS complex were frequent. ST was of normal contour unless specified as being concave or convex. Convexity, concavity and high take-off of ST except in the case of coronary occlusion are of questionable significance. In no case was digitalis taken for at least two weeks prior to the taking of the electrocardiographic tracings.

Precordial leads were used in every case. We employed the new method advised by the Committee on Precordial Leads of the American and British Heart Associations. Lead 4F was used. Deviations from the normal were noted in many instances. The observations relative to these precordial leads will comprise the subject matter for another report.

The functional tests showed that practically all the miners studied had abnormal acceleration of the pulse rate after slight exertion, such as climbing two steps up and down from five to seven times. Along with the acceleration of the pulse rate they experienced marked dyspnea, in some cases so marked that an estimation of the vital capacity could not be made. In seven cases the pulse rate decreased after deep inspiration; in the

rest it either remained about the same or became even faster. Normally it should decrease from ten to eighteen beats a minute with the chest held in full inspiration.

SUMMARY AND CONCLUSIONS

Of twenty-five miners studied, sixteen had anthracosilicosis without pulmonary tuberculosis. Nine had either moderately advanced or far advanced pulmonary tuberculosis in addition to anthracosilicosis. They ranged in age from 36 to 67 years, and the duration of their occupation as miners ranged from three to forty years. Roentgenograms of the heart showed that two had cardiac enlargement. Secondary polycythemia and reduction of vital capacity were frequent occurrences. No appreciable variation from the normal venous pressure and pulmonary and complete circulation time was noted.

The electrocardiograms in the majority of instances showed myocardial damage. We feel that electrocardiographic examinations are of distinct value in the study of anthracosilicosis and that these examinations together with the clinical and laboratory observations described in this report would be of value in recognizing early cardiovascular damage secondary to anthracosilicosis with or without complicating tuberculosis.

THE CLINICAL VALUE OF THE ELECTROCARDIOGRAM

AN ANALYSIS OF 100 PRIVATE CASES

SOLOMON STROUSE, M.D.
LOS ANGELES
LOUIS N. KATZ, M.D.
AND
HERBERT F. BINSWANGER, M.D.
CHICAGO

Inevitably, whenever a new procedure of diagnosis or therapy is developed or gains rapid popularity, the pendulum swings too far and the procedure is apt to be employed in clinical practice beyond its indications. This appears to be true of electrocardiography, which recently has rapidly advanced the ability to interpret damage to the heart, especially that variety which accompanies disease of the coronary vascular system. There is a tendency today to rely too much on the electrocardiogram for the final interpretation of the condition of the heart at the expense of a careful history and an accurate clinical examination of the patient. The fault is less applicable to the cardiologist than to the general practitioner. In many places this trend has gone so far that surgeons require a routine preoperative tracing, believing incorrectly that it will by itself establish the margin of cardiac safety before operation. Eventually this overswing will rectify itself, but the tendency should be checked early so that overenthusiasm will not bring discredit to the real value of the electrocardiogram.

Experience has shown that, when electrocardiography is indicated, considerably more information can be obtained by the use of serial curves with the inclusion of chest leads. This fact became apparent to us both in the course of our clinical private practice and in the course of electrocardiographic interpretation, and it therefore seemed desirable to test it more accurately by systematically reviewing a series of private patients who had been followed for many years and on whom many electrocardiograms had been taken.

The advantage of studying private rather than clinic patients obviously lies in the ability to carry through more sustained and continuous observation. Thus, some of the records used in this study were begun twenty-five years ago for patients who have been under constant supervision, and some of these patients have had ten or more electrocardiograms. The many problems in diagnosis, therapy and, especially, prognosis arising in the course of private practice present a more intensive opportunity for appraisal of the ultimate value of various complementary aids than is possible when the study is limited to data collected by many observers.

The purpose of an assay such as ours would be defeated by studying patients selected on the basis of the electrocardiographic evidence or of the necropsy. While both methods have been useful and several excellent reports of such studies have appeared, they place the emphasis in the wrong place as far as an assay of the value of the electrocardiogram to the patient is concerned. We are convinced that studies such as ours are essential and should be pursued further if the practical value of this objective aid to clinical practice is finally to be determined.

METHOD

One hundred clinical records with electrocardiograms were selected at random, without reference to diagnosis, from our files on private patients. We believe that this series represents a fair sample of cases in a general medical practice.

The clinical records and the electrocardiograms were studied independently. First the patient's records were reviewed, the clinical course of each patient was abstracted and the important developments were noted. Then all the electrocardiograms were reviewed and reinterpreted without regard to original interpretations or clinical notes. The data so assembled were restudied, and from the combined notes an attempt was made (1) to see how closely the electrocardiographic evidence approximated the clinical impression and (2) when there was sharp divergence between this evidence and the clinical impression, to determine from the subsequent course of the patient's illness which was more nearly correct and, if there was an error, in what direction it lay. Another review was then made with particular attention to records showing disagreement between the electrocardiograms and the actual course of events.

RESULTS

Statistical treatment of 100 miscellaneous records gives but little information. Nevertheless, some value is obtained from a tabular summary of our correlation, as is shown in the accompanying table. These figures and others given are intended merely as an indication of trend. In this series no case of rheumatic heart disease and only one of syphilitic heart disease was found. The majority of patients grouped themselves into (1) those complaining of precordial pain or distress, (2) those having diabetes mellitus, hypertension or generalized arteriosclerosis and (3) those requiring electrocardiograms to help exclude the possibility of disease of the heart. In this last group are included (*a*) patients with diseases such as cholelithiasis, bronchial asthma and arthritis and (*b*)

Aided by the A. D. Nast Fund for Cardiac Research.
From the Department of Medicine and the Cardiovascular Department, Michael Reese Hospital, Chicago.

patients with vague symptoms and signs on whom the electrocardiogram was taken as a routine in differential diagnosis.

ROUTINE ELECTROCARDIOGRAMS IN THE ABSENCE OF CLINICAL EVIDENCE OF HEART DISEASE

With regard to the last group, our study suggests that only rarely does a routine electrocardiogram aid the clinician in arriving at a judgment of the condition of the heart. Occasionally the nature of an arrhythmia will be diagnosed by the electrocardiogram or the clinical impression will be confirmed or altered and, depending on the nature of the arrhythmia, the prognosis will be modified. In the arteriosclerotic age group, serial electrocardiograms were an important index of the aging processes in the coronary blood vessels and sometimes seemed to indicate these changes before any clinical evidence was manifest. Furthermore, the rate of change of the contour of the electrocardiogram when a series is taken aids in judging the rate of progress of such coronary disease. We have abundant evidence showing that slight electrocardiographic changes occur from year to year in patients who give no other evidence of a changing status. This coincides with the results obtained from analyses initiated on the basis of electrocardiographic contour.[1] Therefore we firmly believe that the periodic examination of patients more than 40 years of age should include an electrocardiogram with two or more chest leads and that such examinations should be repeated yearly.

Correlation of Electrocardiographic Interpretation in 100 Cases with the Conclusion Arrived at from the Clinical Evidence

Electrocardiographic Interpretation	Total Number of Cases in Group	Number of Cases in Which Electrocardiographic Evidence	
		Coincided with Clinical Evidence	Differed from Clinical Evidence
A. Within normal limits	23	16	7
B. Probably within normal limits	3	3	0
C. Borderline record	9	9	0
D. Probably abnormal	11	8	3
E. Definitely abnormal	54	46	8
Total	100	82	18

Positive evidence, even when slight, usually indicates underlying pathologic changes in the heart, although these may be only transitory reversible abnormalities. Pardee [2] recently has found a similar correlation between electrocardiographic and postmortem observations. Sometimes, with patients having diseases elsewhere than in the heart, the differentiation of cardiac from extracardiac factors may be aided by the electrocardiogram.

In systemic diseases in which heart disease of an arteriosclerotic nature is common, the need for periodic examination with electrocardiograms is even greater. The electrocardiogram properly correlated with the clinical observations aids prognostically in judging the progress of the coronary disease. Furthermore, in the case of hypertension, serial electrocardiograms may aid in determining the presence and progression of hypertrophy; but as a rule x-ray and clinical evidence is much better.

In the foregoing discussion we take for granted that the interpretation is made by a competent medical electrocardiographer on the objective evidence present in the electrocardiogram. Great care must be taken to pay attention to those minutiae which are of significance without reading into the electrocardiogram more than is present. These "minutiae" consist primarily of changes in the contour and direction of the QRS complex, the level of the ST segment and the direction, size and shape of the T wave, as well as the peculiar forms seen in cases of excessive treatment with digitalis and of coronary insufficiency.[1] Particular attention should also be paid to auriculoventricular and intraventricular block.

THE ELECTROCARDIOGRAM AS AN AID IN EVALUATING SUBSTERNAL PAIN AND DISTRESS

A much more serious problem arises with regard to patients with substernal pain or distress, a striking and common clinical phenomenon. These symptoms are listed by Smith, Rathe and Paul [3] among the five major symptoms of coronary insufficiency. These authors state that 54 per cent of their patients, in whom the initial symptom was angina of effort, later developed coronary thrombosis. Saphir, Priest, Hamburger and Katz,[4] in a study of thirty-four cases in which autopsy was performed, showed that half their patients with proved coronary occlusion had had pain referable to the heart. The current literature contains many comments and much disagreement as to the incidence of pain before or during a coronary closure. Levine,[5] for example, has expressed the view that a careful history will reveal a story of pain in the vast majority of instances.

Naturally the incidence of substernal pain will depend on how the material for study is selected. The frequency of pain or distress will be less when the material is selected from a series of necropsies or from a series of electrocardiograms than when the study is initiated by selecting a series of patients. The last method of approach presents the best opportunity for diligent inquiry concerning precordial discomfort. This is particularly true of private practice, in which long clinical observation is possible. In hospital practice many patients are seen under circumstances in which it is not possible to secure a complete history. The true incidence of precordial pain can be estimated more accurately from a series such as we studied, in which more careful histories can be obtained. In our series, of a total of forty-two patients whose condition was diagnosed as coronary occlusion, all but two complained of substernal distress at some time in the past or during the episode. Even these two patients might have had pain.

Since the majority of our patients were studied because of pain of varying intensity, the major portion of this study resolves itself into an inquiry on the significance of substernal pain. Probably no more serious problem confronts the private practitioner than the determination of the cause of chest pain. The reorganization of the mode of life of the patient depends on the correctness of the diagnosis. In each of our cases a careful history and comprehensive physical examination were made before the electrocardiograms were taken. Since no practitioner can hope to attain

1. Behning, A., and Katz, L. N.: The Four Lead Electrocardiogram in Coronary Sclerosis, Am. J. M. Sc. **189**: 833, 1935; The Four Lead Electrocardiogram in Cases of Recent Coronary Occlusion, Arch. Int. Med. **61**: 241 (Feb.) 1938.
2. Pardee, H. E. B.: Relation of Myocardial Disease to Abnormalities of the Ventricular Complex of the Electrocardiogram, Am. Heart J. **15**: 28, 1938.
3. Smith, F. M.; Rathe, H. W., and Paul, W. D.: Observations on the Clinical Course of Coronary Artery Disease, J. A. M. A. **105**: 2 (July 6) 1935.
4. Saphir, O.; Priest, W. S.; Hamburger, W. W., and Katz, L. N.: Coronary Arteriosclerosis, Coronary Thrombosis and Resulting Myocardial Changes, Am. Heart J. **10**: 567 and 762, 1935.
5. Levine, S. A.: Angina Pectoris and Its Relation to Coronary Artery Disease, New England J. Med. **210**: 743, 1938.

perfect efficiency in the diagnosis of precordial distress, the real problem lies in the ability of the electrocardiogram to assist in cases of doubtful diagnosis by helping to determine whether or not the heart is diseased.

Chest pain, as is well known, is not always due to coronary disease or coronary insufficiency. Pain may arise because of so-called psychoneurotic tendencies, as in neurocirculatory asthenia. It may be occupational, as in typists. It may be due to diseases of the spine or nerve roots, diaphragmatic hernia, abdominal diseases or lesions of lung or pleura. It is common with cardiospasm. Careful clinical observation is always needed to disclose all possible extracardiac causes of precordial pain. With the milder and atypical forms of chest pain the electrocardiogram will often be of value, but it is not always diagnostic, since (1) it is possible that organic heart disease may be present and the pain still be due to some other cause and (2) chest pain of cardiac origin does occur in some cases even in the absence of electrocardiographic abnormalities. Furthermore, in the more serious cases of sudden collapse, abnormalities may be found even when no coronary closure is present because the collapse may itself cause acute coronary insufficiency. However, subsequent electrocardiograms will help to disclose whether or not a myocardial infarction has developed.

Our study revealed three facts in this connection: 1. A single electrocardiogram unless it gives specifically positive results has no clinical value. 2. Positive electrocardiographic evidence will not always be of prognostic value, since in several instances the clinical picture and subsequent course gave no evidence of progressive myocardial disease. 3. Successive changes in serial electrocardiograms are the most important diagnostic aids of electrocardiography, particularly when chest leads are included. Many patients in our series have had a normal electrocardiogram immediately after an attack diagnosed clinically as angina pectoris. This is not surprising, since, as is well known, the abnormalities in the electrocardiogram quickly disappear when the attack is over. These normal records cannot be interpreted as an assurance of safety, and the clinical picture cannot be ignored. This is well illustrated by the history of a man aged 59 who was given a thorough physical examination, including the taking of an electrocardiogram, and showed nothing abnormal, yet two weeks later had a severe attack of angina pectoris. The electrocardiogram was normal immediately after the attack. Nevertheless the patient was put to bed on the basis of the clinical evidence and ordered to restrict his activities. Four weeks later he had a fatal attack of coronary occlusion with a typically diagnostic electrocardiogram.

This is not an unusual situation, but it serves to illustrate the importance of recognizing that electrocardiography in the presence of clinically definite angina pectoris fails to give evidence of underlying coronary disease between or even during attacks in about 25 per cent of all cases. Exercise tests help to increase the frequency with which coronary disease may be diagnosed from the electrocardiogram, but even when such tests are positive, normal five lead electrocardiograms may be obtained. This is equally true for patients with less definite precordial distress. It might be well to point out that the mildness or severity of the symptoms is not the significant factor in making a prognosis. Even a long series of electrocardiograms may not give evidence of coronary disease until the patient has a sudden coronary occlusion. It follows that the clinician should never disregard definite or suggestive clinical observations because of negative electrocardiographic evidence. This is particularly true because coronary occlusion may occur without warning in the presence of a long standing negative evidence in the history, clinical picture and electrocardiograms.

This point of view should not be interpreted as an indictment against the electrocardiogram; it simply emphasizes that when reliance is placed exclusively on the electrocardiogram, without considering the clinical picture, serious errors are bound to occur. Ideally, the electrocardiogram or the series should be viewed objectively, the clinical picture should be assayed and then the two should be checked with each other, both reviewed again and then, and then only, a final judgment made. There is no short cut for clinical and common sense.

The cases in which the history, physical examination and clinical course caused us the greatest doubt and the gravest concern were unfortunately those in which the electrocardiograms were likewise of doubtful significance. To illustrate these difficulties we cite the case report of a man seen between the ages of 31 and 39 who had typical angina of effort and whose examinations revealed no physical defect. At least three excellent cardiologists saw this man in consultation, agreeing on a probable diagnosis of angina pectoris or small coronary occlusions. Five electrocardiograms were taken in the course of six years, and all but one were normal. He died at the age of 39 from carcinoma of the pancreas. The coronary arteries at autopsy showed only slight sclerosis. Even though the patient was constantly under observation, with frequent bouts of precordial pain, no objective evidence was obtained by any method of examination warranting a positive diagnosis of coronary disease. The slight coronary sclerosis found at autopsy may have been the explanation of the clinical picture.

Since approximately one half of the patients with substernal distress on effort later have coronary thrombosis, the physician's diagnostic efforts would be greatly aided by a definite diagnostic procedure. The electrocardiogram offers the best complementary aid but cannot be considered 100 per cent efficient. This opinion is well supported by our series and by reports of others.

Another patient, with an almost identical clinical history, illustrates the positive value of serial electrocardiograms. In 1928, at the age of 50, he first complained of definite precordial distress on effort, which has continued to the present. A series of ten electrocardiograms, starting in 1928, is attached to his records. The tracings of 1928, 1933 and February 1934 are normal. During this time he was having precordial pain on effort. Sept. 20, 1934, a more severe but less definite "attack" occurred. Electrocardiograms taken twelve hours afterward showed definite abnormalities. The S-T segment was depressed in all leads, T_3 was inverted, QRS_3 was taller, there was first degree auriculoventricular block, $S\text{-}T_4$ was iso-electric and horizontal and T_4 was smaller. In four days there was definite restoration toward normal, which continued through October 2. An electrocardiographic diagnosis of a small posterior myocardial infarct was made, confirming our clinical impression of atypical coronary occlusion. Since this attack the patient has been leading a restricted life but still has angina of effort. Electrocardiograms taken in 1936, 1937 and 1938 are normal. In short, a patient with constant more or less

severe anginal symptoms had many electrocardiograms taken in a ten year period, all of which were normal except a series of three taken during a more severe episode. In this case the serial electrocardiograms completed the diagnosis of coronary sclerosis with a small occlusion.

Evidence that coronary occlusion is rare in women who are not hypertensive or diabetic receives considerable support from our series of women, some of whom have been observed from ten to twenty-five years. Despite the complaint of indefinite precordial distress, clinical and electrocardiographic examination showed no deviation from normal and several of these women are still alive and active in their eighth decade.

By contrast we have observations on a few women who had indefinite precordial distress with normal electrocardiograms but who later had diabetes or hypertension. These patients showed changing electrocardiograms corresponding to their changing clinical conditions; most of them had final attacks of coronary occlusion.

Both groups indicate the great value of the electrocardiogram in substantiating clinical diagnoses and in establishing prognoses. This was true for women to a much greater extent than for men, as established statistical information would lead one to expect. Emphasis is again placed on the importance of serial studies. Unchanging normal electrocardiograms in women are of good prognostic value, whereas changes may indicate underlying pathologic conditions.

There is a more serious and unsatisfactory problem in the case of men with indefinite precordial pains not typically anginal. Although such men should not be separated too sharply from those with the typical anginal syndrome, the clinical problem is distinct. Patients with angina pectoris receive treatment for the condition regardless of the electrocardiographic evidence, but it is not always easy to determine a method of living for a man with indefinite precordial pains. In a few of our cases the serial electrocardiograms gave evidence of slowly progressive coronary disease, but in most of them (twelve) the electrocardiograms were either normal or on the borderline. Although patients have been followed for years, electrocardiographic evidence has been essentially negative or doubtful. We do not feel confident that such negative evidence is conclusive in ruling out the presence of coronary disease. Even though in the six cases of our series in which autopsy was performed the condition of the coronary arteries had been diagnosed correctly ante mortem by electrocardiograms, the autopsy studies of other authors [4] indicate that coronary disease may be present without previous clinical or electrocardiographic manifestations. Therefore we believe it important to emphasize that a long series of electrocardiograms presenting negative or doubtful evidence does not by any means absolutely preclude the possibility of coronary artery disease.

INTERPRETATION OF THE ELECTROCARDIOGRAM

One of the difficulties encountered in interpreting the electrocardiogram is that of making the objective final judgment intelligible to the clinician. After some experience it has become the practice of one of us (L. N. K.) to make five gradations in the interpretation, to which the following significance has been attached:

1. "Within normal limits" means that the record is not abnormal for the age considered.

2. "Probably within normal limits" means that the record shows some deviation from normal but little significance need be attached to it.

3. "Borderline record" indicates that the record is on the borderline between normal and abnormal and may be of little value to the clinician in determining whether or not there is organic disease.

4. "Probably abnormal" indicates that there are probably abnormalities and that the tracing should carry some weight in making the clinical interpretation.

5. "Definitely abnormal" indicates definite abnormality not to be dismissed lightly.

These five gradations are an attempt at objective quantitative interpretation of the electrocardiogram independent of the clinical evidence. The clinician, aware of this evidence, should find the proper importance to be attached to the electrocardiogram. In no sense are these interpretations to be considered as a substitute for the clinical interpretation; they are rather to be considered as one part of the evidence in finally arriving at a complete clinical assay of the condition.

Certain forms of abnormality gain particular significance, viz. the characteristic curve of coronary insufficiency, of digitalis excess, of auriculoventricular block, of intraventicular block, of auricular fibrillation, of electrical alternans and of multiple premature systoles of several foci of origin. Experience has shown that special significance in most but not all instances can be attached when these particular findings are present in the electrocardiograms.

As the accompanying table shows, the purely objective interpretation of the electrocardiogram independent of the clinical evidence is far from a 100 per cent accurate process. For instance, seven of twenty-six patients with normal or probably normal electrocardiograms showed definite clinical evidence of heart disease at the time or indicated its presence from the subsequent course. Practically all of these had only three limb leads, without chest leads, and most had only one record. Several, however, had serial records and four leads without showing electrocardiographic evidence of cardiac damage. In nine patients with borderline electrocardiographic changes, the electrocardiogram was obviously of no value. More significant to us is the fact that eleven of the sixty-five patients with definitely abnormal curves had no clinical evidence of heart disease during the entire period of observation, although two had intraventricular block. For these eleven patients only a single record was obtained or, when a series was taken, the serial curves did not vary significantly. We can only conclude that a definitely abnormal electrocardiogram may not infrequently be associated with subclinical cardiac involvement and that if the electrocardiographic curve remains stationary the clinical course may be benign. It is important to recognize this fact; otherwise too much significance will be attached to electrocardiographic abnormalities.

In short, this study has demonstrated that, while the electrocardiogram is a useful tool in clinical practice, it constitutes only one part of the clinical examination, and that it must be correlated with the rest of the examination.

We should like to close by cautioning the clinical practitioner to resist the temptation to allow the electrocardiogram to make his diagnosis and prognosis for him. If he avoids this pitfall, a definite place in clinical practice is assured for this important clinical aid.

BALANTIDIASIS

MARTIN D. YOUNG, Sc.D.
Junior Zoologist, United States Public Health Service
COLUMBIA, S. C.

The rarity of reported cases of balantidiasis in the medical literature makes any new focus of infection worthy of note. Therefore when an active infection with Balantidium coli was found in a patient at the South Carolina State Hospital, an investigation was instituted to determine the prevalence of the parasite in a selected group of patients. The patients examined were those suffering from diarrhea and those with a mental condition which tolerated untidiness, as it was felt that if additional infections were present they were most likely to be found among these patients.

Usually two fecal specimens from each patient were examined, but the stools of patients found to be infected with Balantidium coli were examined repeatedly. A simple saline smear preparation was used. No technics of concentration of parasites were employed. A total of seven infections were found among the 142 patients examined. This represents an incidence of 4.93 per cent. Since only two examinations were made and the appearance of the parasites in the stools is irregular, as is shown hereafter, it is possible that some infections were not found.

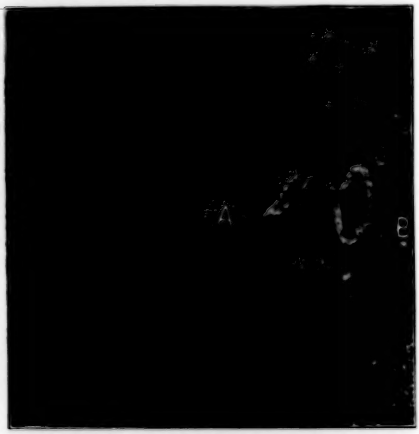

Fig. 1.—Appearance of living trophozoite of Balantidium coli (*A*) in a fecal smear. An ovum of Trichuris trichiura (*B*) is shown for comparison. A negative print is used for contrast (× 300 approximately).

REPORT OF CASES

Case 1.—E. A., a white woman aged 61, was mentally deteriorated, anemic, mute, bedridden and untidy when admitted to the hospital in July 1935. The mental diagnosis on admission was psychosis with cerebral arteriosclerosis. About one year after admission diarrhea developed, which became chronic and sometimes produced a dozen stools daily. The stools were usually small and watery and contained flakes of mucus. Medication for diarrhea had not alleviated the condition. On examination of a loose stool in February 1938, numerous trophozoites of Balantidium coli were seen. Ova of Trichuris trichiura (whipworm) and Necator americanus (hookworm) and larvae of Strongyloides stercoralis were present also. Repeated fecal examinations over a three weeks period revealed that the recovery of Balantidium coli was variable; some stools did not show parasites. Examination of well formed stools usually gave negative results, whereas loose and diarrheic stools contained large numbers of the parasites.

At no time were cysts or precystic forms of Balantidium coli observed. There was little variation in the occurrence of worm ova and larvae in the stools during the period of examination.

Case 2.—D. H., a white woman aged 42, on admission in 1920 had dementia praecox of the catatonic type. She was very untidy and filthy, with marked diarrhea. Balantidium coli was observed in the stool in April 1938. Ova of Trichuris trichiura and Necator americanus and larvae of Strongyloides stercoralis were present also. Eighty-nine examinations were made in the 177 days from April 18 to October 12, at which time treatment was instituted; trophozoites of Balantidium coli were found seventy-seven times and cysts eight times.

Case 3.—H. K., a white woman aged 33, who had been in the hospital nine years, had dementia praecox of the hebephrenic type. She had a ravenous appetite, refused to talk, was very untidy and soiled herself on many occasions. She had chronic diarrhea of at least one year's duration and occasional dysentery. Balantidium coli was first observed in April 1938. Ova of Trichuris trichiura and Necator americanus and larvae of Strongyloides stercoralis were present also. Over a period of 180 days, thirty-five stools were examined; trophozoites of Balantidium coli were found thirty-three times. Numerous cysts were found in two stools.

An examination of the blood during the latter part of the observation period showed leukocytes 28,500, with polymorphonuclears 77 per cent, lymphocytes 21 per cent and eosinophils 2 per cent; erythrocytes 3,900,000, and hemoglobin 43 per cent.

Case 4.—S. H., a white girl, was 19 years old when committed in 1932, with a diagnosis of dementia praecox of the catatonic type. She had had pellagra. She was untidy and destructive of property. Recent marked diarrhea, with from eight to ten stools a day, together with an occasional dysenteric stool, led to the first examination of the stools. Numerous trophozoites of Balantidium coli were seen, together with ova of Trichuris trichiura and Necator americanus and larvae of Strongyloides stercoralis.

Over a nineteen day period, eleven examinations of stools were made; trophozoites of Balantidium coli were found seven times. During this period no cysts were seen.

A blood count revealed leukocytes 10,250, with polymorphonuclears 65 per cent and lymphocytes 35 per cent; erythrocytes 2,110,000, and hemoglobin 32 per cent.

Case 5.—J. T., a white woman aged 53, had been in the hospital intermittently since 1910, the mental diagnosis being mental deficiency (imbecility) without psychosis. In 1932 she received treatment for diarrhea. Since 1932 tuberculosis had been present. Recently she had been showing marked diarrhea. Oct. 22, 1938, she passed eight or ten stools, and the following day three stools were passed within an hour. Examination of one of these diarrheic stools revealed Balantidium coli and ova of Trichuris trichiura and Necator americanus. Two stools examined during one week both showed trophozoites of Balantidium coli.

Examination of the blood showed leukocytes 17,400, with polymorphonuclears 57 per cent, lymphocytes 39 per cent and eosinophils 4 per cent; erythrocytes 3,900,000, and hemoglobin 63 per cent.

Case 6.—A. L., a white woman aged 50 who had been in the hospital for eleven years, had dementia praecox of the catatonic type. She was noisy, destructive, untidy and filthy in her habits. She had chronic diarrhea, which had recently become marked. Balantidium coli was observed in a purged stool after treatment with oil of chenopodium. Ova of Trichuris

From the Williams Malaria Research Laboratory of the United States Public Health Service, located at the South Carolina State Hospital.
Dr. Bruce Mayne, U. S. Public Health Service, prepared the photomicrographs, and Drs. John Cuttino and Coyt Ham, South Carolina State Hospital, cooperated in the securing of materials.

trichiura and Necator americanus and larvae of Strongyloides stercoralis were also present. Over a period of five days, four examinations of stools were made and trophozoites of Balantidium coli were found each time. Three stools contained cysts also.

Examination of the blood revealed leukocytes 11,050, with polymorphonuclears 68 per cent, lymphocytes 31 per cent and

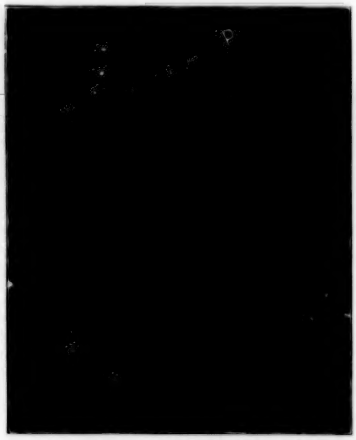

Fig. 2.—The trophozoite of figure 1 enlarged to show the peristome (*P*) (× 750 approximately).

eosinophils 1 per cent; erythrocytes 3,810,000, and hemoglobin 57 per cent.

CASE 7.—J. W., a white woman aged 31, with dementia praecox of the catatonic type, was noisy, destructive, untidy and filthy in her habits and mentally was markedly deteriorated. She had had diarrhea accompanied by anemia for about two years. Oil of chenopodium was given for worms and living trophozoites of Balantidium coli were found in the purged stools. Hookworm and ova of Trichuris trichiura and larvae of Strongyloides stercoralis were present also. Four examinations over a period of four days each showed Balantidium coli. No cysts were observed.

Examination of the blood revealed leukocytes 9,950, with polymorphonuclears 76 per cent and lymphocytes 24 per cent, erythrocytes 3,600,000 and hemoglobin 60 per cent.

MORPHOLOGY

Balantidium coli is a ciliated protozoan parasite (figs. 1, 2 and 3). It is the largest protozoon parasitic in man and is generally thought to be the only ciliate parasitic in human beings.

The parasites are oval to egg shaped. The body is uniformly covered with cilia, the animal swimming with a forward rotary motion. It has a funnel-shaped cytostome near the anterior end through which it feeds. Two contractile vacuoles are present. Body wastes are discharged through the anal opening, the cytopyge. In stained specimens the small micronucleus, embedded in the shelter of the large dumb-bell shaped macronucleus, can be seen.

Measurements of 100 living quiescent trophozoites were made from one of the specimens. The length ranged from 54 to 146 microns, with a mean of 91.64 microns. The breadth ranged from 37 to 100 microns, with a mean of 57.25 microns.

The cysts are spherical to ovoid-spherical, many of them appearing as perfect spheres (fig. 4). They are protected by a transparent double wall. The parasite can frequently be seen rotating slowly within the cysts.

Twenty cysts from one stool specimen were measured. The length ranged from 47 to 64 microns, with a mean of 54.6 microns. The breadth ranged from 45 to 57 microns, with a mean of 51.5 microns.

LIFE CYCLE AND PATHOGENICITY

The accepted theory of infection is that cysts are swallowed. After excysting, the parasites establish themselves in the large intestine. The parasites are capable of penetrating the intestinal mucosa to form flask-shaped ulcers, similar to those produced by Endamoeba histolytica, which may undermine the epithelium (figs. 5 and 6). Extensive ulceration results in large areas of necrotic epithelium, which is shed and passed to the outside with blood, thus giving rise to balantidial dysentery. Active trophozoites are passed in large numbers during this stage.

In the present series of cases, 145 examinations of stools were made. Trophozoites were found 127 times,

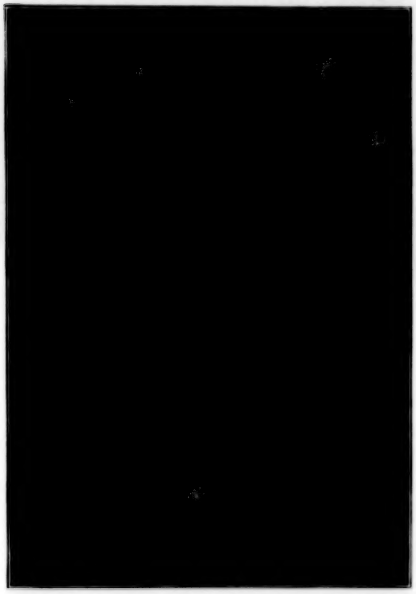

Fig. 3.—High magnification of the trophozoite of figure 2, showing cilia (*C*) and peristome region (*P*); × 1,000.

or in 87.5 per cent of the examinations. Cysts were found thirteen times, or in 8.9 per cent of the examinations. Usually if the stool was decidedly diarrheic only trophozoites could be found. The cysts were found in the firmer stools and, when present, were usually seen in great numbers, sometimes almost to the exclusion of the trophozoites.

7 113
1939

EPIDEMIOLOGY

Nisbet [1] in reviewing the American literature found the following cases reported: three from Louisiana, four from Arkansas, three from New York, two from North Carolina and one each from Iowa, Minnesota, Mississippi, Oklahoma (the patient had lived in Kansas also), Massachusetts and Maryland. In his report, Nisbet described a case from North Carolina.

Fig. 4.—Living cyst of Balantidium coli in a fecal smear. (*A*) cyst wall, (*B*) outline of macronucleus (× 1,340 approximately).

Logan [2] reported four cases from Minnesota. In 1924 McEwen [3] reported a case from Kansas in which the symptoms extended over twenty-six years. Ford [4] reported a case from Washington and referred to a case reported from New Mexico by Gant [5] in 1915. In 1932 Mendelson [6] found the infection in a native of New Mexico, and Scott [7] in 1935 reported five cases of nonsymptomatic infection from West Virginia.

Thus until the present report, thirty-two cases had been reported from sixteen states in this country. Little [8] in 1931, reporting a case from Canada, stated that fewer than 250 cases had been reported in the medical literature.

Meleney (personal communication in May 1938) reported two cases in Tennessee. These two cases and the seven cases from South Carolina reported in this paper make a total of forty-one infections found in eighteen states.

TREATMENT

The long list of medicaments which have been tried and recommended for this infection speaks for the lack of a universally accepted treatment. Cures supposedly effected with one drug have not been duplicated in the hands of other clinicians. Therefore when the present study was begun there was no drug that could be relied on as being specific for these parasites.

Because of the similarity in pathogenicity of balantidiasis to amebiasis and because both causative agents are protozoa, it was decided to try a drug that has given good results in the treatment of amebiasis, viz., carbarsone. Patient 1, the first treated, was old and very weak, and therefore the drug was given in smaller doses than those employed in the treatment of amebiasis. One and one-half grains (0.1 Gm.) a day was given for four days, after which the treatment was interrupted for unrelated causes. Treatment was started again nine days later; on the fourth day the dose was increased to 3 grains a day (0.2 Gm.), which was given for five days. On the next to the last day of treatment the patient received 5¼ grains (0.3 Gm.) in two doses and on the last day 3¾ grains (0.24 Gm.) in one dose. The total time from the beginning to the end of treatment was twenty-two days, and the patient received a total of 34½ grains (2.2 Gm.) of carbarsone given in fourteen days.

Trophozoites of Balantidium coli were found throughout the course of the treatment, but on the last day most of them appeared dead. Daily examinations for three weeks after the termination of therapy failed to disclose parasites. Examination of the stools gave negative results for five months, after which the examinations were discontinued.

Fig. 5.—Section of a large intestine of man showing ulceration caused by Balantidium coli. Nests of the parasites (*A*) can be seen at the base of the ulcer. (Material from the Philippines.)

Patient *2* was given 0.25 Gm. twice a day for ten days. Living balantidia were seen the first day after treatment. The next specimen was obtained on the sixth day of treatment and showed only dead balantidia. For one month thereafter no balantidia were seen.

The other patients are now under treatment.

The carbarsone seemed to have little effect on the parasitic helminths present.

1. Nisbet, W. O.: A Case of Balantidial Coli Infection, South. M. J. **13**: 403-406 (June) 1920.
2. Logan, A. H.: Balantidium Coli and Pernicious Anemia: Report of Four Cases, Am. J. M. Sc. **162**: 668-674 (Nov.) 1921.
3. McEwen, F. J.: Balantidium Colitis, M. Clin. North America **7**: 1289-1294, (Jan.) 1924.
4. Ford, D. R.: Balantidial Dysentery with Report of a Case, Northwest Med. **24**: 558-559, 1925.
5. Gant, S. G.: Diarrheal, Inflammatory, Obstructive and Parasitic Diseases of the Gastrointestinal Tract, Philadelphia, W. B. Saunders Company, 1915.
6. Mendelson, R. W.: Balantidic Dysenteria, Southwest Med. **16**: 156-158, 1932.
7. Scott, T. G.: Infestation with Balantidium Coli: Five Concurrent Nonsymptomatic Cases, M. Bull. Vet. Admin. **11**: 368 (April) 1935.
8. Little, J. L.: Case of Balantidium Dysentery in Canada, Canad. M. A. J. **25**: 653-657, 1931.

Meleney, in a communication to me during August 1938, gave the results of treatment in one of the two cases found in Tennessee. The patient was a housewife living on a farm. She had been treated for pernicious anemia for four years. She had simple diarrhea ostensibly associated with the pernicious anemia. Balantidia were found in the stool in January 1926. The first course of treatment consisted of the administration of carbarsone by mouth, 0.25 Gm. twice a day for eight days. The balantidia disappeared from the stools and the diarrhea stopped. Dilute hydrochloric acid was given at the same time and may have been responsible for cessation of the diarrhea. The patient was readmitted to the hospital in April 1936, and balantidia were again present in stools. The diarrhea had recurred also. The patient was then treated with carbarsone, 0.25 Gm. being given by mouth twice a day for ten days and carbarsone enemas being given on alternate nights for four treatments. The latter part of the treatment consisted of a cleansing water enema followed by a retention enema with 2.0 Gm. of carbarsone dissolved in 200 cc. of 1 per cent solution of sodium bicarbonate. The balantidia disappeared after the third enema, which was given on the sixth day of the oral treatment. Stools were examined two weeks and three weeks later; no balantidia were found. Examination of the stools two years later (July 1938) revealed no balantidia.

In the South Carolina infections, as noted, oral treatment with carbarsone has been more effective than in Meleney's case. The stools of the first patient treated here were shown to be free from balantidia at all examinations made over a period of five months after the treatment. The stools of the second patient were still free from the parasites after a month. However, a number of patients must be followed over a long period to establish definitely that carbarsone provides a cure.

Oil of chenopodium administered orally to several patients was not efficacious in ridding them of the balantidia. One dose each was given to patients 4, 6 and 7, and two doses were given to patient 2. The balantidia were neither eliminated nor appreciably diminished in numbers by this drug, being found continuously before, during and after its administration.

Cort [9] reported twelve Balantidium coli infections cured by rectal administration of oil of chenopodium. However, Serra [10] reported the death of a child following the treatment used by Cort. It appears therefore that this drug, like many others, is not satisfactory for Balantidium coli infections.

COMMENT

Diarrhea and, occasionally, dysentery accompanied the infections reported. As the patients also harbored worms, which are capable of producing these symptoms, it cannot be said that the diarrhea and dysentery were due entirely to the balantidia.

However, in many of the reported cases in which Balantidium coli was the only etiologic agent, diarrhea and dysentery were present. The pathogenicity of balantidiasis has been definitely established by Walker [11] and others. This disease should merit more serious consideration.

The reports of Balantidium coli infections show the widest diversity in locality, climate, race, sex and age. Because of the wide scattering of the few human cases reported and because in many cases the infection has been associated with hogs, which show a high rate of infection, the idea is often expressed in the literature that man probably contracts the parasite from this animal rather than from human sources.

With this in mind, when the first infection was found here, the personal history of the patient was searched carefully. It was found that she had lived on a farm for about forty-five years and had sometimes helped in the preparation of meats from freshly slaughtered hogs. Because of this possible source of infection, five members of her immediate family, who had lived under identical conditions, were given one fecal examination. None were found to be infected and none showed symptoms. Also it must be borne in mind that the symptoms of diarrhea did not occur in this case until after hospitalization of about one year.

Fig. 6.—Two of the parasites of figure 5 enlarged. The dumb-bell shaped macronucleus (*B*) can be seen in one of them.

Detailed personal histories and examinations of the families of the other patients were not obtainable.

Because of their mental condition, all the infected patients tolerated untidiness, both personal and environ-

9. Cort, E. C.: Infection with Balantidium Coli: Twelve Cases Treated with Oil of Chenopodium, J. A. M. A. **90**: 1430-1431 (May 5) 1928.
10. Serra, A.: Balantidial Dysentery in Child: Death Following Rectal Administration of Chenopodium, Porto Rico J. Pub. Health & Trop. Med. **6**: 443-444 (June) 1931.
11. Walker, E. L.: Experimental Balantidiasis, Philippine J. Sc. **8**: 333-350, 1913.

mental. The clothing might become contaminated and often it was difficult to collect sufficient feces for an examination. The exercise grounds were polluted. This type of patient often puts rocks, leaves, sticks, grass, dirt and other débris into his mouth. Thus the factors necessary for the transfer of the infection from one person to another were present.

Although the chance of contracting the infection from hogs cannot be ruled out, it seems likely that the infections in these cases were contracted from human sources.

The factors for transmission of Balantidium coli are undoubtedly present in many places, especially where there is crowding or other conditions which make strict personal hygiene difficult. It is also likely that man is more frequently infected with this parasite than the few reported cases would indicate, many infections being overlooked or misdiagnosed.

SUMMARY AND CONCLUSIONS

1. Seven infections with Balantidium coli in white women were observed by me in South Carolina and two cases were found in Tennessee by Meleney.

2. The infected patients had chronic diarrhea and occasionally dysentery. Trichuris trichiura, Necator americanus and Strongyloides stercoralis were present also, and consequently the symptoms may not have been due entirely to the balantidia.

3. Frequent examinations of the stools were made in cases of infection. In 145 examinations, trophozoites were found 127 times, a percentage of 87.5. Cysts were found thirteen times, a percentage of 8.9.

4. Epidemiologic evidence indicates that the present infections were contracted from human sources rather than from hogs; swine are generally thought to be the source for most infections in man.

5. The balantidia disappeared from the stools of two patients treated with carbarsone. The stools of one patient were still free after five months. One month had elapsed since the treatment of the second and no balantidia had been seen. Oil of chenopodium given orally was not efficacious.

6. Few reports of this disease occur in the literature. Previous to this report, thirty-two cases had been reported from sixteen states. This report adds nine more cases, from two states.

7. The evidence indicates that the disease may be more prevalent than is reported.

Postoffice Box 1344.

ADDENDUM.—Since this manuscript was submitted for publication, two additional infections of Balantidium coli have been found at this hospital. This brings the total number of infections reported from South Carolina to nine.

Do the Neurotic Become Psychotic?—The hypothesis has frequently been advanced that many neurotic patients are in reality only early psychotic cases whose condition has not yet become acute. The essence of the theory is that certain neurotic conditions are in reality only early forms of psychosis. In an attempt to give evidence to this point Ross followed up his neurotic patients to find which were later certified as psychotic. Of the 1,186 neurotic patients, but fifty subsequently developed a psychosis, from which Ross feels that there is a possibility of a psychoses following a neurosis but that there is no ground for believing that psychoses and neurosis are different degrees of the same thing.—Landis, Carney, and Page, James D.: Modern Society and Mental Disease, New York, Farrar & Rinehart, Inc., 1938.

GRANULOCYTOPENIA CAUSED BY SULFAPYRIDINE IN CHILDREN

NATHAN ROSENTHAL, M.D.
AND
PETER VOGEL, M.D.
NEW YORK

Practically every case of granulocytopenia can be traced to an underlying sensitivity to certain drugs, such as aminopyrine, arsphenamine, dinitrophenol and, more recently, sulfanilamide. The introduction of sulfapyridine as a therapeutic agent in pneumonia has led to its widespread use. Wien,[1] experimenting with mice and rats, concluded that sulfapyridine is one fourth as toxic as sulfanilamide and that it has no apparent effect on the hemopoietic system. There is reason to believe that sulfapyridine is as toxic as sulfanilamide for the bone marrow, or more toxic, since we have observed ten cases of granulocytopenia (including one in a child) in the past two years. However, we have in the past few months observed three cases of granulocytopenia in children following the administration of sulfapyridine. This, in fact, is the purpose of the present communication—to call attention to the danger of employing sulfapyridine over prolonged or intermittent periods unless careful and frequent study is made of the blood picture. Two cases of granulocytopenia which occurred in adults during the administration of sulfapyridine have been reported in the British literature.[2] Barnett [3] and Long [4] have each mentioned a case which came under their observation.

There is no doubt that the following cases of granulocytopenia resulted directly from the use of this drug:

REPORT OF CASES

CASE 1.—*Recurrent pneumonia; monocytic granulocytopenia following intermittent use of sulfapyridine; recovery.*

John G., a baby aged 1 year, was admitted because of diarrhea Feb. 26, 1939, to the Lincoln Hospital.[5]

Signs of pneumonia, which were not verified by x-ray examination, developed over the left lower lobe. A total of 6 Gm. of sulfapyridine was given with good results. The child was discharged well after eight days of normal temperature. Two days later, at his home, an infection of the upper respiratory tract developed with nasal discharge and fever. After a week of elevation of temperature and failure to improve, the baby was again admitted to the hospital.

On admission the temperature was 102 F. The child appeared acutely ill and had a slight cough. There was dulness over the right lower lobe and a reddened left ear drum. A total of 8 Gm. of sulfapyridine was given in seven days. On the eleventh day after admission (four days after sulfapyridine had been stopped) the patient became fretful and began to vomit. The temperature rose to 102 F. and then dropped to normal within twenty-four hours. Vomiting continued for four days and then stopped; it was followed by diarrhea, which continued. There was a steady loss of weight, from 20½ pounds (9.3 Kg.)

1. Wien, R.: The Toxicity of 2(Para-Aminobenzenesulfonamido) Pyridine, Quart. J. Pharmacol. **11**: 217-224 (April-June) 1938.
2. Johnston, F. D.: Agranulocytosis Following Treatment with M. & B. 693, Lancet **2**: 1200 (Nov. 19) 1938. Coxon, R. V., and Forbes, J. R.: Agranulocytic Angina Following Administration of M. & B. 693, ibid. **2**: 1412-1413 (Dec. 17) 1938.
3. Barnett, H. L.; Hartmann, A. F.; Perley, A. M., and Ruhoff, M. B.: The Treatment of Pneumococcic Infections in Infants and Children with Sulfapyridine, J. A. M. A. **112**: 518 (Feb. 11) 1939.
4. Long, P. H.: Sulfapyridine, J. A. M. A. **112**: 538 (Feb. 11) 1939.
5. From the pediatric service of Dr. H. S. Altman.

on admission to 18 pounds (8.2 Kg.) during the third week. The stools became less watery and more frequent.

During the fourth week after admission, signs of pneumonia again appeared over the right lower lobe. Before a report of the blood count could be obtained, the patient was given 1.25 Gm. of sulfapyridine. A blood count April 17 revealed 4,000 white blood cells, with 10 per cent polymorphonuclears. April 18 examination of the blood revealed hemoglobin 110 per cent, red cells 5,200,000, white cells 1,100, platelets 210,000 and reticulocytes less than 0.5 per cent. The differential count was nonsegmented polymorphonuclears 6 per cent, segmented neutrophils 2 per cent, lymphocytes 60 per cent, monocytes 30 per cent, basophils 1 per cent and myelocytes 1 per cent.

Aspiration of the sternal marrow revealed 60,000 nucleated cells and 88 megakaryocytes per cubic millimeter. The differential count was myeloblasts 1.4 per cent, myelocytes 71 per cent (fig. 1), eosinophilic myelocytes 1.8 per cent, nonsegmented neutrophils 1.2 per cent, segmented neutrophils 1.4 per cent, eosinophils 2.4 per cent, basophils 0.2 per cent, lymphocytes 3.2 per cent, hematogones 1.6 per cent, reticulum cells 0.2 per cent, megakaryocytes 0.2 per cent, erythroblasts 3.6 per cent and normoblasts 1.8 per cent.

The baby was given two blood transfusions and three injections of liver extract.

A blood count April 20 revealed 4,200 white cells. The differential count revealed nonsegmented neutrophils 4 per cent, segmented neutrophils 3 per cent, lymphocytes 37 per cent, monocytes 54 per cent (fig. 2) and myelocytes 2 per cent. The baby improved gradually and the rest of his stay in the hospital was uneventful.

CASE 2.—*Staphylococcus aureus osteomyelitis, treated continuously with sulfapyridine (95 Gm.), followed by lymphocytic granulocytopenia; fatal.*

H. W., a Negro boy aged 10 years, was admitted to the orthopedic service of Mount Sinai Hospital[6] March 28, 1939, because of pain in the right shoulder of three days' duration. Three years previously, in an automobile accident, the patient suffered a fracture of the right clavicle. Two months prior

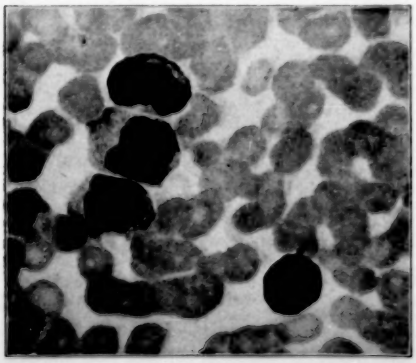

Fig. 1 (case 1).—Blood smear, monocytic granulocytopenia, magnification 1,000 diameters. Three monocytes and a plasma cell are shown at edge of smear.

to admission several furuncles appeared on his neck; these subsided without incision and drainage. Three days before admission he began to have pain in the right shoulder, which became worse. The temperature rose to 102.5 F.

The child appeared toxic, with rapid respirations and pulse; the temperature was 103.8 F. There were typical manifestations of osteomyelitis of the right humerus. An operation was performed and the diagnosis was substantiated. The smear and culture at the time of operation yielded Staphylococcus aureus. For a few days following the operation the child continued to have fever. The temperature became normal on the fourth day. Treatment with sulfapyridine (1 Gm. every four hours) was started March 29, a total of 6 Gm. being administered

Fig. 2 (case 1).—Bone marrow, monocytic granulocytopenia, magnification 1,000 diameters. Three myelocytes with "toxic" granules, a myeloblast and a plasma cell are shown.

daily and continued until April 13. The patient received a total of 95 Gm.

On admission, examination of the blood revealed hemoglobin 95 per cent, white cells 16,700, nonsegmented neutrophils 8 per cent, segmented neutrophils 78 per cent, lymphocytes 6 per cent and monocytes 8 per cent. Several blood counts done before April 13 showed moderate leukocytosis and polymucleosis. However, April 14 examination of the blood revealed hemoglobin 69 per cent, red cells 4,250,000, white cells 3,400, platelets 180,000, nonsegmented neutrophils 10 per cent segmented neutrophils 14 per cent, lymphocytes 71 per cent, monocytes 3 per cent and plasma cells 2 per cent. The temperature rose to 102 F. and remained elevated. The patient was given a transfusion immediately and later injections of pentnucleotide.

Examination of the blood April 17 revealed hemoglobin 84 per cent, red cells 5,100,000, white cells 700, platelets 240,000, and lymphocytes 100 per cent. On April 18 the blood showed a faint trace of sulfapyridine. Examination April 19 showed hemoglobin 72 per cent, red cells 4,960,000, white cells 300, platelets 160,000 and reticulocytes 1 per cent.

Aspiration of the sternal marrow revealed a total nucleated count of 25,000 cells (normal 200,000) and the following differential count: myelocytes 3.5 per cent (normal 30 per cent), segmented neutrophils 0.5 per cent (normal 20 per cent), lymphocytes 32 per cent (normal 15 per cent), hematogones

6. Dr. Seth Selig gave us permission to publish a report of this case.

3.5 per cent, plasma cells 1 per cent, reticulum cells 2 per cent, erythroblasts 1.5 per cent and normoblasts 56 per cent (normal 35 per cent).

The patient was given transfusions, but the white blood cells continued to decrease in number and the temperature reached 105 and 106 F. and remained there. His condition became worse and he died April 20. Permission for autopsy could not be obtained.

Case 3.—*Hypoplastic anemia following intermittent use of sulfapyridine in a case of whooping cough and pneumonia; fatal.*

G. S., a Negro girl aged 4 years, was admitted Jan. 25, 1939, to Willard Parker Hospital [7] because of whooping cough. February 5 pneumonia developed, for which sulfapyridine was given, 2 Gm. for the first dose and 0.5 Gm. every four hours, 3 Gm. a day being given up to February 13—a total of 20 Gm. The temperature dropped to normal February 7 but rose two days later.

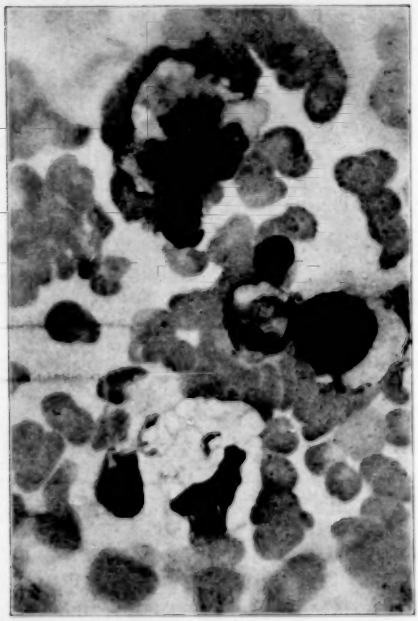

Fig. 3 (case 3).—Bone marrow hypoplastic anemia; magnification 1,000 diameters. Reticulo-endothelial cells (vacuolated) and two normoblasts are shown.

February 15 signs of pneumonia again appeared and sulfapyridine was again given, 3 Gm. daily, without effect. The temperature dropped to normal February 19 but the drug was continued until February 21. Pneumococcus serum type VI was also given.

The temperature rose on Februaray 21 and at that time the white count was 2,000, with 96 per cent lymphocytes. February 25 examination of the blood showed hemoglobin 64 per cent, red cells 3,400,000, white cells 1,100, platelets 105,000, lymphocytes 99 per cent and plasma cells 1 per cent. Aspiration of the sternal marrow revealed a total nucleated count of 33,800 per cubic millimeter and megakaryocytes 11 per cubic millimeter. The differential count revealed myeloblasts 2.6 per cent, myelocytes 2.6 per cent, lymphocytes 37.3 per cent, hematogones 6 per cent, reticulum cells 5.3 per cent, megaloblasts 0.7 per cent, erythroblasts 10 per cent and normoblasts 35.5 per cent. The child's condition became worse, the temperature became elevated and, in spite of repeated transfusions, he continued to go down hill and died March 1.

A complete postmortem examination was obtained, the details of which will be reported later by Dr. Vera B. Dolgopol.

7. From the service of Dr. Jerome Kohn.

COMMENT

Sulfapyridine is a valuable drug in the treatment of pneumonia in adults and children.[8] It is usually effective within two or three days.

In addition to the continuous nausea which usually follows the ingestion of sulfapyridine, dangerous toxic complications may arise, of which granulocytopenia and jaundice are the most important symptoms, especially in children. Strict precautions should therefore be exercised, and the blood picture, icterus index and bone marrow (obtained by sternal puncture) should be examined. A reduction in the number of white blood cells to 3,000 or 4,000 should be viewed as a danger signal. Administration of the drug should be stopped at this time and should certainly not be resumed until the number of white blood cells returns to normal. Its use beyond this period—especially if the temperature does not drop or if there is no improvement in the course of the disease—may in fact be regarded as ineffectual and possibly as dangerous. Sulfapyridine should be discontinued also if it induces anemia or if jaundice appears. The drug appears to be more dangerous if given over a long period or intermittently in various types of infection, including pneumonia in children.

It is important to remember that the toxic action may continue for several days after the drug has been discontinued. In case 2, for example, traces of sulfapyridine were still present in the blood five days after it had been administered. The necessity of following the trend of the blood picture and of making occasional observations of the bone marrow in all cases after prolonged use of the drug thus becomes apparent.

There is some variation of the effect of sulfapyridine on the bone marrow which is reflected in the blood picture. This resembles to a great extent the toxic action of neoarsphenamine.[9] With both the bone marrow changes are rather definite and vary from a maturation arrest to a distinct, almost complete, suppression or hypoplasia of all the elements.

Case 1 is an example of only a moderate toxic action of sulfapyridine on the bone marrow inducing so-called maturation arrest. Although there is a marked decrease in the total nucleated count (60,000) there is a relative increase in myelocytes (71 per cent) with marked toxic granulation. The mature neutrophils are considerably diminished, to 2.6 per cent (normal 20 per cent). The blood picture showed a relative monocytosis up to 54 per cent. This is the type for which a good prognosis may be predicted; as has been previously reported, there is a high incidence of recovery in such cases.[10] In case 2 the toxic action was apparently more marked with a severe depression of the myeloid elements, with relative

8. Barnett, Hartmann, Perley and Ruhoff,[3] Long.[4]

9. Rosenthal, Nathan: Chapter on Aplastic Anemia in Downey's Handbook of Hematology, New York, Paul B. Hoeber, Inc., 1938.

10. Rosenthal, Nathan, and Abel, H. A.: The Significance of Monocytes in Agranulocytosis (Leukogenic Infectious Monocytosis) Am. J. Clin. Path. 6: 205-230 (May) 1936.

increase in lymphocytes and normoblasts. The effect of the drug was still more marked in case 3, in which there was hypoplasia of all elements and an increase in the number of reticulo-endothelial cells (fig. 3).

It is important to follow the bone marrow as well as the blood picture in children who are receiving sulfapyridine for a prolonged or intermittent period. Attention should be paid to the cellular content, which, according to Vogel and Bassen,[11] should be about 200,000 per cubic millimeter. The finding of some diminution, especially when the content has dropped to less than 100,000, calls for caution in the further use of the drug.

Like sulfanilamide, sulfapyridine may exert a marked hemolytic action on the red blood cells of adults [12] and of children.[13] Brahdy [13] called our attention to the following case:

An Armenian boy aged 9 years was admitted to the Pediatric service of the Mount Vernon Hospital [14] Feb. 20, 1939, with a history of fever, cough and pain in the chest of four days' duration. On admission signs of pneumonia (confirmed by x-ray examination) were found in the left upper lobe. The sputum showed a type I pneumococcus. The patient was given a total of 9 Gm. of sulfapyridine over a period of three days. A blood count February 21 showed hemoglobin 63 per cent, red cells 3,800,000, white cells 14,000, nonsegmented polymorphonuclears 14 per cent, segmented polymorphonuclears 68 per cent and lymphocytes 18 per cent. Jaundice was noted on the third afternoon and the drug was immediately stopped. The patient was given intravenous injections of dextrose, and the following day (February 24) the blood count revealed hemoglobin 20 per cent, red cells 1,400,000, white cells 22,600, nonsegmented polymorphonuclears 21 per cent, segmented polymorphonuclears 53 per cent, lymphocytes 24 per cent and monocytes 2 per cent. Following two transfusions the hemoglobin content rose to 43 per cent, with 1,750,000 red blood cells, 24,200 white blood cells and the following differential count: nonsegmented polymorphonuclears 17 per cent, segmented polymorphonuclears 78 per cent, lymphocytes 14 per cent and monocytes 1 per cent.

Again, as with sulfanilamide, the hemolytic reaction resulting from sulfapyridine, as exemplified in this case, occurs within a short time (about three days). This is in contradistinction to the development of granulocytopenia, which follows the prolonged or intermittent use of sulfanilamide or sulfapyridine.

51 East Ninetieth Street.

11. Vogel, Peter, and Bassen, F. A.: Sternal Marrow of Children in Normal and Pathological States, Am. J. Dis. Child. 57:245-268 (Feb.) 1939.
12. Erf, L. A.: Personal communication to the authors.
13. Brahdy, M. B.: Personal communication to the authors.
14. From the service of Dr. Walter Brundage.

The Special Function of the Skin.—It is gradually being recognized that the skin, far more than a mere protective covering of the body, is a separate and important organ, with physiological functions of its own that affect the body as a whole in a variety of ways. . . . That the skin has chemical functions of importance is apparent from investigations such as those of Folin, Trimble and Newman, who determined a rapid accumulation of sugar in the skin of animals when glucose was injected intravenously. The sugar concentration in the skin rapidly became almost equal to that in the blood. Trimble and Carey later, studying human skin from normal and diabetic subjects, found that elevation of sugar concentrations in the blood was accompanied by an absolute increase of the sugar in the skin, an increase far greater than that determinable in muscle tissue.—Zinsser, Hans; Enders, John F., and Fothergill, LeRoy D.: Immunity Principles and Application in Medicine and Public Health, New York, Macmillan Company, 1939.

Clinical Notes, Suggestions and New Instruments

PROSTATECTOMY AT THE AGE OF 110

J. BAYARD CLARK, M.D., NEW YORK

First of all, I wish to state the grounds of my belief as to this man's age, for it is here that the center of interest lies in this extraordinary case.

Aside from his own assertion and that of his family that he was born in the year 1827 in slavery in the state of Virginia, that he was not married until he was 40 and that his oldest son, if alive, would now be 70, I have made careful inquiries as to his supposed age from a number of reliable citizens in the town of Greenwich, Conn., where he became a resident after the Civil War.

A contractor for whom he worked on a building operation in 1900 or 1901 states that he was past 70 at that time. Another source of information is a remarkable old gentleman in his ninety-seventh year for whom the patient often worked and who knows him well. His belief is that he is well past 105, and a number of other trustworthy persons who seem to have known him most of their lives—two lawyers, four physicians and one clergyman over 80—place him as beyond 107 or 108, or even at the man's own estimate of 110. Further than this, for obvious reasons, it is hardly possible to authenticate his years.

Fig. 1.—Six months after operation, still smiling.

It is, of course, a well known fact that many Negroes in slavery lived to be extremely old and beyond the age of this man. When one considers the possibility of their direct descent, in the early part of the last century, from a primitive African stock living in a natural way and untouched by the diseases of civilization, the fact of positive health and extreme longevity is not so strange. A cursory examination of the literature, however, revealed no report of a prostatectomy having been done in the case of any one reaching a hundred years of age.

This patient was admitted to the hospital May 19, 1938, suffering from acute urinary retention of four days' duration. He stated that there had been no previous difficulty or urinary disturbance. The abdomen was distended and the dome of the bladder reached to the umbilicus. The prostate was smooth, unevenly lobulated, elastic and about the size of a tangerine.

A soft catheter entered easily and gradual decompression was instituted.

His past history disclosed no pathologic condition. He maintained that he had never been ill but that some ten or twelve years before he was laid up for a few days because of a dislocated shoulder, which is still somewhat stiff.

As to his manner of living, he seems to have been moderate in all things except in the matter of paternity, having had twenty-two children, four of whom are still living. He eats sparingly of a diet of vegetables and milk. He smokes a pipe once a day. His work has been mainly outdoors and in later years that of road construction, the patient having had much experience in blasting operations.

Physical examination disclosed a thin, well muscled body. The skin had a healthy appearance. The teeth were mostly discolored stumps. The lungs were emphysematous. The heart

Read before the Section of Genito-Urinary Surgery, the New York Academy of Medicine, Jan. 18, 1939.

sounds were somewhat weak and irregular, with no murmurs. The blood pressure was 140 systolic, 90 diastolic. Examination of the abdomen revealed a reducible inguinal hernia. The external genitalia were firm and surprisingly well developed.

Mentally he was alert, cheerful and responsive, having lost none of the lively sense of fun peculiar to his race. His eyesight was poor but his hearing was acute.

Examination of the urine and blood, including chemical analysis, gave essentially negative results.

Here was a peculiar picture of normality outside the usual experience, even with comparatively young patients in their seventies.

Taking it all together, it was difficult to resist the belief that he was a perfectly good surgical risk, so at the end of an uneventful week of catheter drainage it was decided to drain the bladder suprapubically. This was skilfully done by Dr. W. J. Washburn May 26 under local anesthesia, and a mushroom drainage tube was inserted. Save for a slight elevation of temperature the following day the patient suffered no reaction.

Suprapubic drainage was continued without incident until June 14, when prostatectomy was done.

Fig. 2.—Six months after operation, still walking.

Notwithstanding the conviction that the man was fully able to go through with the operation, there was still the lingering consciousness of stepping on untested ground which might give way when it was least expected. With this in mind, we reduced the operative procedure to its simplest form. Under light anesthesia with avertin with amylene hydrate the patient was brought sleeping to the operating room. The enucleation, which was a little more difficult than I had expected it to be, took between six and seven minutes. During this period the anesthesia was deepened with nitrous oxide gas. Two lobes, one a little larger than the other, were cleanly removed with very little bleeding. The prostatic bed was lightly packed with rib dam and the operation was over. The patient was returned to bed in excellent condition and given a clysis of 1,000 cc. of 5 per cent dextrose.

On waking the following morning after his operation he demanded a "square meal." On the third morning I found him propped up in bed joyfully puffing away at an ancient pipe. For five days his postoperative behavior was uneventful. Then something happened.

A temperature of 102.2 F. and a dry cough were reported. Examination disclosed dulness at the base of the right lung, and this was verified by the examinations made with a portable x-ray machine. There were no other physical signs or symptoms. Though he neither looked nor acted sick, precautions were taken against what might be. The next day his temperature reached 103 F. but he remained as cheerful as ever. There was no change in the picture except that the "dry cough" seemed to have vanished. Then of a sudden the gloom was lifted when a tender and moderately swollen right epididymis was discovered. One could contend with that at any age. The following day brought a level temperature and a subsiding epididymitis.

The moral of this case seems to be that perhaps the first hundred years of life are the worst after all.

Without further incident the suprapubic wound continued to close, and by July 1 he was passing urine by the urethra. The urine by this time was slightly cloudy with pus, but he showed no symptoms of infection. By July 5 he was up and about the ward. July 10 he was discharged from the hospital.

The specimen weighed 30 Gm. The lobes were fibrous, containing glandular areas. There was a little scattered lymphocytic exudate. The diagnosis was benign hypertrophy of the prostate, with mild chronic prostatitis.

When at the end of July the patient reported at the hospital for a checkup he had no complaints and was enthusiastic about the free flow of urine. The urine was clear and the amount of residual urine was 40 cc. In September he was in his usual cheerful and healthy condition. The urine was clear and there was no residual urine. His visit, Jan. 12, 1939, showed no change from the previous examination. He laughed heartily when I gently chided him for coming out in freezing weather without an overcoat. This patient was still alive and very well June 26, 1939, one year after the operation.

140 East Fifty-Fourth Street.

HEMATOMA OF ABDOMINAL WALL OCCURRING IN A CASE OF WHOOPING COUGH

HERBERT E. BOWLES, M.D., HONOLULU, T. H.

Mrs. C., a widow aged 56, white, the mother of two healthy children now aged 22 and 26, had always been exceptionally well and for years had played forty-five holes of golf in one day twice a week. The patient had been taking care of two grandchildren who were suffering from typical pertussis. Three weeks before her present illness she contracted a classic case of whooping cough. Frequently paroxysms of severe coughing ensued.

Following one of these attacks during the night of May 12, 1936, the patient was seized with a sudden knife-like pain in the lower left quadrant of the abdomen and was admitted to the Queen's Hospital in Honolulu in profound shock. The pulse was rapid and thready and the entire body was bathed in a clammy sweat. In addition, respirations were shallow and sighing in type, and a tender mass was palpable in the left lower quadrant of the abdomen. On vaginal examination a tender tumor could be felt in the region of the left adnexa but slightly anterior to where adnexal tumors are usually found.

She was treated for shock by another physician, who gave her intravenous dextrose and saline solution and a blood transfusion. On admission the leukocytes numbered 9,300 with 66 per cent neutrophils. The following morning, shock had disappeared but she had a rigid, tender abdomen and the tumor mass was even more pronounced. The white cells now numbered 6,950. In addition, marked ecchymosis was noted in the left groin, pubes and vulva, around the anus and in the left buttock. The bluish discoloration had also extended up to and around the umbilicus. After several days with only bed rest the pain and rigidity grew less and she returned home. The tumor remained the same size and was very tender.

A vaginal examination two weeks after the onset of her illness revealed a large hypertrophic cervix, a hard, enlarged uterus (the size of a two months pregnancy) and a mass in the left adnexal region the size of a baseball, fixed, tender and protruding anteriorly. The ecchymosis showed evidences of clearing. Preoperative diagnosis was uncertain, but we believed that we were dealing with a left ovarian cyst twisted on its pedicle, or a hemorrhagic ovarian cyst. Pertussis vaccine was administered once a day for one week prior to operation. A general examination was negative except for a blood pressure of 190 systolic, 110 diastolic. The Wassermann reaction of the blood was negative.

Under nitrous oxide anesthesia a hypertrophic cystic cervix was amputated by Dr. G. C. Milnor. Following this the peritoneal cavity was explored through a midline subumbilical incision. All pelvic viscera appeared normal. The slightly enlarged fibrotic uterus was left alone. An elongated but otherwise normal appendix was removed. The examining hand then felt a swelling lying under the left rectus muscle and indenting the peritoneum markedly from above. The peritoneum was

closed and the lower portion of the left rectus sheath was then incised. Behind the muscle and arising from the left deep epigastric artery was a partly encapsulated semiorganized collection of black blood. Two hundred and fifty cc. of clots was evacuated, and the cavity was drained by a strip of rubber dam. No shredding or rupture of the rectus muscle was noted. Recovery was uneventful.

COMMENT

The case is presented as a matter of interest because of the likelihood of confounding it with various gynecologic conditions. So far as we can ascertain, hematoma of the abdominal wall occurring in whooping cough has not been previously reported, though Robertson [1] stated that it occurs in tetanus, typhus and miliary tuberculosis and that in elderly women obesity, pendulous abdomen and atheroma of the blood vessels undoubtedly play a part.

Most of the cases reported in the literature as spontaneous hematoma of the abdominal wall are not truly spontaneous, as careful reading of the history shows. This case cannot be called a spontaneous one since the accident immediately followed and was probably precipitated by the coughing spell. Other reports on the subject have been presented by Wohlgemuth,[2] Maxwell,[3] Halperin,[4] Hartmann,[5] Culbertson[6] and others. Lasch[7] has shown that the hemorrhages in whooping cough are due to actual changes in vessel walls, which he thinks are of toxi-infectious origin. In our case atherosclerosis probably played a part.

SUMMARY

1. A case of hematoma from rupture of the left deep espigastric artery occurred in a woman aged 56 suffering from whooping cough. The rupture followed a paroxysm of coughing.

2. Most similar cases are not truly spontaneous, and search will usually reveal some form of associated violence.

881 Young Street at Thomas Square.

113
1939

TYMPANIC MEMBRANE DESTROYED BY JAPANESE BEETLE

MAX KIMBRIO, M.D., HUNTINGTON, N. Y.

C. L., a man aged 37, complained that two weeks previously a foreign body had entered his right ear and that he had not been able to hear well since.

Ear drops had been instilled within twenty-four hours by the nurse at his place of employment. At the expiration of two weeks he reported to his physician, Dr. Patiky, who referred him to me to remove what was found to be a Japanese beetle.

I had to amputate the wings first and then remove the body. The legs or biting equipment remained behind, stuck fast in the ear drum. They were removed after some difficulty. A perforation involving a very large part of the drum was present. There was a scanty odorless discharge. Hearing to all intents and purposes was normal. The patient gave no history of any previous ear trouble.

Since the Japanese beetle is herbivorous, it is difficult to understand his appetite for human ear drums. I have been unable to find in the literature any report of the destruction of an ear drum by a beetle which lives on plants.

22 High Street.

1. Robertson, H. M.: Hematoma of Abdominal Wall (with Rupture of Rectus Abdominis Muscle) Simulating Intra-Abdominal Tumor, Canad. M. A. J. **30**: 606 (June) 1937.
2. Wohlgemuth, K.: Ueber die subcutane Ruptur des Musculus rectus abdominis und der Arteria epigastrica: Spontanes Bauchdeckenhämatome, Arch. f. klin. Chir. **122**: 649, 1922.
3. Maxwell, A. F.: Spontaneous Hematoma of Abdominal Wall in Women, California & West. Med. **30**: 407 (June) 1929.
4. Halperin, George: Spontaneous Hematoma of the Abdominal Wall, Surg., Gynec. & Obst. **47**: 861 (Dec.) 1928.
5. Hartmann, H.: La rupture partielle des muscles droits de l'abdomen, Presse méd. **25**: 241 (April 26) 1917.
6. Culbertson, Carey: Hematoma Occurring Spontaneously in Sheath of Rectus Abdominis Muscle, J. A. M. A. **85**: 1955 (Dec. 19) 1925.
7. Lasch, W.: Pathogenesis of Hemorrhage in Whooping Cough, Monatschr. f. Kinderh. **28**: 441 (Aug.) 1924.

Council on Pharmacy and Chemistry and Council on Foods

THE COUNCIL ON PHARMACY AND CHEMISTRY AND THE COUNCIL ON FOODS HAVE AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT. THE DATE OF THE MEETING AT WHICH THE QUESTIONS WERE FIRST CONSIDERED WAS DEC. 9, 1938. THE REPORT, HOWEVER, REPRESENTS NOT ONLY ACTIONS TAKEN AT THE MEETING BUT OPINIONS ARRIVED AT FOLLOWING SUBSEQUENT DISCUSSION BY THE COUNCILS. THE REPORT, AS PUBLISHED, REPRESENTS THE COUNCILS' OPINIONS AS OF JULY 1939.

PAUL NICHOLAS LEECH, Secretary
COUNCIL ON PHARMACY AND CHEMISTRY
FRANKLIN C. BING, Secretary
COUNCIL ON FOODS

THE STATUS OF CERTAIN QUESTIONS CONCERNING VITAMINS BASED ON RECOMMENDATION OF THE COOPERATIVE COMMITTEE ON VITAMINS

The Cooperative Committee on Vitamins met at the Association headquarters Dec. 9, 1938. The following members of the Cooperative Committee were present: Dr. S. W. Clausen, Dr. H. N. Cole, Dr. G. R. Cowgill, Dr. Morris Fishbein, Dr. P. C. Jeans, Dr. Irvine McQuarrie, Dr. E. M. Nelson, Dr. L. J. Roberts, Dr. M. S. Rose, Dr. W. C. Rose, Dr. Torald Sollmann, Dr. F. C. Bing and Dr. P. N. Leech. In addition, the following members of the Council on Foods and the Council on Pharmacy and Chemistry were present: Dr. D. P. Barr, Dr. Joseph Brennemann, Dr. J. H. Brown, Dr. E. M. K. Geiling, Dr. E. E. Irons, Dr. H. B. Lewis, Dr. G. W. McCoy, Dr. J. S. McLester, Dr. R. M. Wilder. Also present as guests were Dr. T. G. Klumpp of the Food and Drug Administration, Dr. K. E. Miller of the Federal Trade Commission and Dr. T. D. Spies.

I. Questions Primarily Concerning the Council on Pharmacy and Chemistry

The Council on Pharmacy and Chemistry considered the matter of permissible claims for vitamins under the following classifications:

Permissible claims for vitamin A.

Permissible claims for riboflavin, thiamin chloride and nicotinic acid, including vitamin B complex.

Permissible claims for ascorbic (cevitamic) acid (including relation to arsenical eruptions).

Permissible claims for vitamin D and vitamin A and D preparations.

Based on this program the Council issued the following revised statement on permissible claims for vitamins and authorized its inclusion in N. N. R. for 1939:

VITAMINS

The investigations of nutrition that have been initiated since the second decade of the present century have afforded an entirely new outlook on many disorders, some of which have long been suspected to be of dietary origin. This is due to the scientific demonstration that in addition to the long recognized proximate principles—the proteins, carbohydrates and fats—which yield the energy requisite for life and activity and which, along with certain inorganic elements, form the structure of the tissues and the fluids of the organism, other factors also are essential for the preservation of bodily well being and physiologic function. They are at present commonly designated as vitamins.

The absence of any one of the vitamins from a diet which is satisfactory in other respects leads to the development of a syndrome which is called a "deficiency disease." These diseases may be as striking in their manifestations as are the direct result of underfeeding (caloric deficiency) or deprivation of essential inorganic elements such as iodine, iron, calcium or phosphorus. A striking illustration of a "deficiency disease" is presented by scurvy. This can be averted or effectively cured by the inclusion of foods which contain vitamin C (ascorbic acid) in the diet. It has been clearly established by convincing

experiments that the prophylactic or remedial agent—the antiscorbutic substance—is a definite chemical entity having the composition $C_6H_8O_6$. The vitamin is present in many articles used as food, such as green vegetables and fruits, yet lacking in others, such as the common cereals and grains. Ascorbic acid is readily destroyed by heat under certain conditions, notably in an alkaline medium and in the presence of oxygen. However, foods can be processed without serious loss of ascorbic acid if precautions are taken to exclude air and if the reaction of the food is not unfavorable for the preservation of the vitamin.

The foregoing illustration will suffice to indicate the characteristics of a vitamin—a substance essential for maintenance of normal metabolic functions, not identical with the more familiar nutrients, not synthesized in the human body, and therefore dependent on an exogenous supply, sometimes more labile than the foodstuffs proper and hence subject to deterioration, and distributed variously among the edible parts of animals and plants. A number of products having the properties of vitamins have been isolated or synthesized.

For convenience the designations vitamins A, B, C and D, and so on have arisen. Scurvy, beriberi, rickets, pellagra and xerophthalmia have been attributed with considerable experimental certainty to the lack of specific vitamins; the protective or curative substances are accordingly sometimes spoken of as the antiscorbutic vitamin (C), the antirachitic vitamin (D), the antineuritic vitamin (B_1), the antixerophthalmic vitamin (A), and so on. Detailed accounts of the physiology of the vitamins can now be found in the newest textbooks on physiologic chemistry and nutrition. The problems raised thereby are the subject of active discussion and extensive investigation, so that with respect to many features only tentative conclusions should be announced at this time.

While some helpful chemical and physical methods for determining the quantity of vitamins present in a given product are now available, for conclusive evidence we must rely on biologic assays. To facilitate such assays and to make for uniform expression of vitamin content, the Health Organization of the League of Nations has sponsored the preparation and distribution of standards for vitamins A, B_1, C and D. The international unit for each of these vitamins is defined in terms of the biologic activity of a specific quantity of the respective standard. The U. S. P. XI units for vitamins A, B_1 and D are identical in value with the international units.

Although considerable evidence bearing on the subject has accumulated the requirements for vitamins A, B_1, C and D for either infants or adults have not been established except within rather wide limits. Apparently there is no reason why a properly selected diet should not afford an adequate supply of the requisite vitamins. Furthermore, with the exception of pellagra and a possible vitamin B_1 deficiency there is no evidence of a noteworthy prevalence in this country of conditions in adults that might properly be ascribed to a lack of one or more vitamins. However, under circumstances bringing about a highly restricted dietary regimen and leading to "one-sided" diets a relative shortage of some of the vitamins at times arises. In many such instances the situation can be properly corrected by prescription of appropriate foods. Occasionally, and particularly with infants, a corrective result may be more effectively and more speedily secured by the administration of the vitamin itself or products especially rich in the desired vitamin; for example, cod liver oil as a dietary adjunct in the prevention or treatment of rickets, and orange juice or crystalline ascorbic acid in the relief of scurvy.

The chief justification for the recognition of special vitamin-bearing products at present applies to unusual concentrations of the desired potent principle that they may represent or to exceptionally desirable dosage forms. These considerations, which may be modified by the progress of research, have served as criteria in the selection of products offered for inclusion in N. N. R. as products rich in specific vitamins at present recognized to have demonstrable value in clinical practice or human nutrition; or as pure substances such as carotene, which is a precursor of vitamin A, ascorbic acid (crystalline vitamin C), or thiamin chloride (crystalline vitamin B_1).

The Council considered the matter of mixed vitamin therapy and decided that for the present there seems to be no more logical basis for including all or a number of vitamins in one preparation than there is for combining a number of other known dietary essentials in any one pharmaceutical product. Since vitamins A and D occur together in nature, and on the basis of the long clinical experience with cod liver oil the Council accepts products containing these two vitamins. The Council will consider for acceptance vitamin concentrates of the required potency made from a single natural product which may contain more than one of the known vitamins.

VITAMIN A

The term "vitamin A" has been applied to any one of several substances or to a mixture of them producing a certain demonstrable specific physiologic effect. It seems to have been definitely established that there are at least five substances which can produce to some degree this characteristic response in the animal body. These are vitamin A itself, alpha, beta and gamma carotene and cryptoxanthin. The last four of these, the precursors of vitamin A, are produced in the plant kingdom, and ingestion of these substances by most animals results in varying degree (depending on the species of animal and the precursor fed) in the formation of a compound having the empiric formula $C_{20}H_{29}OH$ and to which no other name than vitamin A has been given. The extent to which the different precursors of vitamin A can be converted to vitamin A by different species of animals has not been definitely established. The exact function of vitamin A has not been established, but the pathologic picture which results from varying degrees of deficiency has been the subject of extensive investigation.

The claims recognized under vitamin A shall be recognized under the precursors of vitamin A only under conditions specified elsewhere under Carotene.

Allowable Claims.—1. Evidence for the existence of vitamin A and its role in human nutrition is based on the fact that a characteristic eye disease, usually called xerophthalmia, results from a deficiency of this vitamin.

2. It is generally agreed that the first symptom or at least one of the first clinical symptoms of vitamin A deficiency is night-blindness, or nyctalopia. For this type of night blindness vitamin A is a specific. Cases of nyctalopia exist which do not respond to treatment with vitamin A. These may be due to congenital defects or to other diseases than avitaminosis A. In view of present knowledge, the claim is not acceptable that the administration of vitamin A to drivers of automobiles will diminish the chance of accident from driving at night.

3. Vitamin A is reported to be effective in the treatment of certain types of hyperkeratosis of the skin of persons suffering from severe deficiency of vitamin A.

4. Present indications are that vitamin A is an aid toward the establishing of resistance of the body to infections in general only when there has been a decrease of body reserves of the vitamin and the ingestion of vitamin A is inadequate. It has not been shown to be specific in the prevention of colds, influenza and such infections, nor has it been demonstrated that ingestion of vitamin A far in excess of that necessary for normal body function and readily obtained from a properly selected diet is an aid in preventing various types of infections.

5. A deficiency of vitamin A results in a retardation of growth when body stores of the vitamin have been sufficiently depleted, but it must be borne in mind that vitamin A is no more important in contributing to normal growth than any one of the other vitamins, the essential mineral elements or amino acids. Statements conveying the impression that vitamin A is more important in promoting growth than other food essentials are therefore considered misleading and objectionable.

6. There is at the present time inadequate evidence to warrant the claim that the ingestion of sufficient vitamin A will prevent the formation of renal calculi in man or that it is useful in the treatment of hyperthyroidism, anemia, degenerative conditions of the nervous system, sunburn or ulcerative conditions of the skin.

THE VITAMIN B COMPLEX

The term Vitamin B Complex is applied to a group of substances which have been shown to be constituents of what was formerly called vitamin B. The exact number of these con-

stituents is not known at present but the following have been mentioned in recent discussions of the subject:

Thiamin (vitamin B_1) or Thiamin Chloride (vitamin B_1 hydrochloride), the antiberiberi vitamin which prevents beriberi in man and polyneuritis in animals.

Riboflavin, a compound necessary for growth in chicks and rats, and for the prevention of cataract in rats. It is a component of an oxidation-reduction system of living cells.

Nicotinic Acid (amide), (P-P Factor), a nutritional factor effective in the treatment of human pellagra and curative of blacktongue in dogs.

Filtrate Factor, a factor for the prevention of a nutritional dermatosis in chicks.

Vitamin B_5, a factor necessary for rapid gains in weight and normal nutrition of pigeons.

Vitamin B_6, a factor for the prevention of a specific paralysis in rats and chicks.

Vitamin B_7, a factor necessary for weight maintenance of pigeons.

Vitamin B_8, or, Vitamin H, a factor for the prevention of a nutritional dermatosis in rats.

Factor W, a factor necessary for growth of rats.

The chemical nature of thiamin, riboflavin, nicotinic acid (amide) and vitamin B_6 is known. There is biologic evidence, some convincing and some rather vague, for the other factors named. Only thiamin, nicotinic acid (amide) riboflavin and vitamin B_6 have thus far been definitely shown to be necessary in human nutrition and to be of therapeutic value in human disease.

The use of the term vitamin G has led to considerable confusion. This term should not be used to designate the pellagra-preventive factor. It has been demonstrated that vitamin G as determined by the Bourquin-Sherman procedure is a measure of riboflavin. Since this is the most widely accepted procedure for determining riboflavin content, the Council will for the present recognize claims for vitamin G content on the basis of Bourquin-Sherman units in natural products or concentrates made from them. However, it seems preferable to modify the Bourquin-Sherman technic to the extent of using pure riboflavin as a reference standard so that potency can be expressed in micrograms of riboflavin. There appears to be no necessity of labeling pure preparations of riboflavin to show vitamin G units.

While it has been shown that riboflavin is necessary for the normal nutrition of certain species and has a wide distribution in living cells, there is only limited evidence bearing directly on its role in human nutrition. Recent reports indicate that this substance as well as vitamin B_6 may be of value in the prevention and cure of some of the symptoms frequently associated with pellagra.

THIAMIN (THIAMIN CHLORIDE)

Thiamin is recognized as being of fundamental importance in connection with the disease beriberi. The pure compound was first isolated in 1927. Since that time its chemical constitution has been established and it is now being manufactured synthetically. It is usually prepared as the hydrochloride, thiamin chloride, which has the formula $C_{12}H_{17}ON_4SCl \cdot HCl$.

During the past year the International Conference on Vitamin Standardization adopted crystalline vitamin B_1 hydrochloride as the standard for this vitamin and defined the unit as the biologic activity of 3 micrograms of this standard.

Allowable Claims (Thiamin).—1. Thiamin is of value in correcting and preventing beriberi.

The consensus of the students of beriberi is that this disease is due primarily to an insufficient supply of thiamin. There are conditions which probably could be designated as "latent beriberi"; it does not seem wise at this time to attempt the formation of a definite statement covering such conditions other than that presented in item 7.

2. Thiamin may be cited as of value in correcting and preventing anorexia of dietary origin in certain cases.

There are many causes of anorexia, some referable to infections and the reactions thereto, others to organic disorders, and still others related to faulty diet. Where there is no rather obvious cause of anorexia in question, other than a possible dietary one, it is permissible to claim that thiamin may be of therapeutic value when the condition to be treated is due to a deficiency of that vitamin.

3. Thiamin is of value in securing optimal growth of infants and children.

Citations in the literature support the claim that a suboptimal supply of thiamin results in limitation of growth.

4. The therapeutic use of thiamin chloride may be recommended when there are specific conditions indicating interference with proper assimilation of the vitamin from the food.

The present status of research on the clinical use of thiamin for specific diseases other than beriberi and for infant feeding is such that *definite* claims for therapeutic value in relation to such diseases cannot be recognized. Its use may be indicated, however, in such restricted conditions as pernicious vomiting of pregnancy, tube feedings through a jejunal fistula, and the like, because the foregoing permitted statement applies to such conditions and gives an intelligent basis for such therapy.

5. Claims for concentrates of thiamin offered for clinical use should state the potency in terms of the international unit. The term "concentrate" or a synonym will not be recognized if the product does not exceed a potency of 25 international units per gram (or per cubic centimeter), or if it is a natural product which may have been subjected to a process of dehydration.

6. In connection with medicinal foods acceptable for N. N. R., the claim that a food is valuable because of its thiamin content may be made only if it provides in the quantity of food consumed daily at least 200 units of thiamin.

Any food preparation having less than such an amount cannot be regarded as a noteworthy medicinal source of the vitamin. In the light of present knowledge the daily requirement for thiamin appears to be not less than 50 units (international) for the infant and 200 units (international) for the adult.

7. While it has not been established that thiamin deficiency is the sole cause of conditions described as alcoholic neuritis, the neuritis of pregnancy and the neuritis of pellagra, there is evidence of the value of this vitamin in the treatment of these conditions. Vague representations with respect to the value of thiamin in the treatment of other types of neuritis are not permissible.

8. It appears that there is an increased requirement for thiamin when there is greatly augmented metabolism such as occurs in febrile conditions, hyperthyroidism or vigorous muscular activity.

NICOTINIC ACID AND NICOTINIC ACID AMIDE

When dogs are fed a pellagra-producing diet they develop a disease known as "blacktongue," which is cured by the administration of either nicotinic acid or nicotinic acid amide. For a number of years canine blacktongue has been regarded as an analogue of human pellagra. Because of the apparent relationship of the two diseases the Council voted in 1938 to accept nicotinic acid and nicotinic acid amide "for purposes of standardization and clinical experimentation." Sufficient evidence has now been accumulated to demonstrate the usefulness of these drugs in the treatment of pellagra.

Allowable Claims (Nicotinic Acid).—1. Nicotinic acid (amide) is recognized as a specific only in the treatment of acute pellagra in relapse. Its administration in appropriate doses leads to the disappearance of alimentary, dermal and other lesions characteristic of the disease, to a return to normal of the porphyrin and porphyrin-like pigments of the urine, and to a profound improvement in the mental symptoms when the latter are the result of an inadequate intake of nicotinic acid (amide). Nicotinic acid is without influence on the polyneuritis and certain other symptoms frequently observed in pellagrous patients. In such cases it may be necessary to insure the presence in the diet of foods rich in vitamin B_1 or to administer thiamin chloride. Riboflavin and vitamin B_6 may also be required for the relief of other symptoms not influenced by nicotinic acid or thiamin chloride.

2. Available evidence does not warrant the use of nicotinic acid (amide), riboflavin or vitamin B_6 for prophy-

lactic purposes or the suggestion that these substances be employed as a supplement to the ordinary diet. The protective dose, and the amount which should be present in a well balanced ration, are unknown.

ASCORBIC ACID
(Cevitamic Acid)

There is ample experimental and clinical evidence to show that ascorbic acid in optimal amounts is an essential dietary constituent. Suboptimal amounts result in the development of clinical and pathologic phenomena to which the descriptive term scurvy has been applied.

The chemical nature of the formerly unidentified essential food substance has been discovered. Its empirical formula is $C_6H_8O_6$, ascorbic acid (cevitamic acid), which has been prepared in commercial quantities both from natural sources and through synthesis.

Allowable Claims (Ascorbic Acid).—1. Ascorbic acid is acceptable for the correction and prevention of scurvy. This effect has been established experimentally and by clinical investigation.

2. Definite claims for the therapeutic value of ascorbic acid should be permitted only in relation to scurvy until further clinical or experimental evidence has substantiated its usefulness in other states.

3. It may be permissible under certain conditions to refer to the therapeutic value of ascorbic acid in early and latent scurvy. Convincing clinical evidence has established that this state does occur. It would be well to emphasize the fact that the diagnosis rests, however, on the basis of roentgenologic evidences in the long bones, and possibly failure to excrete an optimal amount of ascorbic acid in the urine.

4. Dental caries, pyorrhea, certain gum infections, anorexia, anemia, undernutrition and infection alone are not in themselves sufficient indications of ascorbic acid deficiency but according to experimental and clinical investigation they may be concomitant signs of ascorbic acid deficiency. Therefore, it is permissible to accept the claim for the therapeutic value of ascorbic acid in these symptomatic conditions *only when* it is definitely stated that they are the consequences of a deficiency or suboptimal amount of ascorbic acid or when there is a pathologic interference with assimilation of the amount necessary for the preservation of health.

5. Unless more convincing evidence is present than is now available, no claim referable to the anti-infective effect of ascorbic acid will be recognized. Secondary infections are characteristic of disturbances of nutrition, particularly in all vitamin deficiency diseases. It has not been established that ascorbic acid has a therapeutic effect which directly influences associated secondary infections in scurvy.

6. Because ascorbic acid is a dietary essential, its administration in concentrated form is of value in conditions in which difficulty in introducing orally or utilizing ordinary foods in the usual way is encountered. Ascorbic acid is accepted as an essential dietary constituent in infant feeding but it should not be accepted for use in the treatment of diseases except according to the conditions mentioned. It is generally administered in the form of an ascorbic acid carrying juice. It may be administered parenterally in concentrated form as sodium ascorbate when persistent vomiting, diarrhea or other conditions prevent the utilization of proper amounts taken orally.

7. Ascorbic acid offered for clinical use must state the potency in terms of the international unit. The international unit for ascorbic acid, which was formerly defined as the vitamin C activity of 0.1 cc. of lemon juice, is now defined as the ascorbic acid activity of 0.05 mg. of ascorbic acid. This is the quantity of ascorbic acid usually found in 0.1 cc. of lemon juice.

8. In the opinion of the Cooperative Committee on Vitamins, adopted by the Council, the claim that a food is valuable because of its ascorbic acid content should be permitted only if it provides a daily intake of at least 250 international units of ascorbic acid.

9. A reasonable general statement regarding allowable claims for ascorbic acid would be as follows:

An optimal amount of ascorbic acid should be supplied at all ages for its therapeutic value in preventing the development of acute or latent scurvy.

Claims for the therapeutic value of ascorbic acid may be accepted when the agent is described as a corrective measure for scurvy due to a demonstrable absence or a suboptimal quantity in the diet, or in cases in which it is definitely known that there is interference with the absorption of an optimal amount.

Advertising of ascorbic acid for such symptoms as failure to gain in weight or stoppage of growth, anorexia, anemia, infections, symptoms referable to the central nervous system or hemorrhagic conditions cannot be accepted unless it is definitely stated that the symptoms are referable to a demonstrable deficiency of ascorbic acid.

The ascorbic acid equivalent or potency in terms of international units should be stated in all dosage claims for ascorbic acid. Ascorbic acid is easily decomposed in presence of certain other substances; therefore, care should be exercised against administering it (or orange juice) in mixtures, or by any procedure which renders it ineffective.

VITAMIN D

The term "vitamin D" is applied to one or more substances which function in the proper utilization of calcium and phosphorus. Vitamin D has been produced in crystalline form as one of the products of ultraviolet irradiation of ergosterol and shown to be a sterol having the formula $C_{28}H_{43}OH$. Two forms of naturally occurring vitamin D have now been isolated and one of these forms is identical with the vitamin D produced by the activation of ergosterol.

Some reports have appeared claiming clinical improvement in chronic arthritis and in certain allergic disorders as a result of the use of massive doses of vitamin D. Critical examination of these reports reveals little to warrant the belief that the clinical effects claimed are specific. There is suggestive clinical evidence that the use of massive doses of vitamin D may cause improvement in some cases of psoriasis, but the effect is not yet well enough established to justify a claim for such use. The Council believes that further studies should be conducted, but because of the possible toxic effects of large doses of vitamin D it is necessary that such studies should be made only in clinics where close supervision is possible. The Council also holds there is not sufficient evidence to warrant the acceptance of viosterol preparations of high potency for use in the treatment of arthritis.

Allowable Claims (Vitamin D).—1. Vitamin D is recognized as a specific in the treatment of infantile rickets, spasmophilia (infantile tetany) and osteomalacia, diseases which are manifestations of abnormal calcium and phosphorus metabolism. Vitamin D is valuable in the prevention as well as in the curative treatment of these diseases. Complications such as renal insufficiency or glandular malfunction may preclude normal response to vitamin D therapy. During acute infections, especially of the gastrointestinal tract, vitamin D may prove ineffective because poorly absorbed.

2. Direct exposure of the skin to ultraviolet rays from the sun or from artificial sources results in the formation of vitamin D within the organism but the Council cannot recognize statements or implications that vitamin D has all beneficial effects of exposure to sunshine.

3. There is clinical evidence to justify the statement that vitamin D plays an important role in tooth formation and maintenance of normal tooth structure, but there is no warrant for the claim that adequate vitamin D intake will insure normal tooth structure or that adequate vitamin D intake will prevent dental caries.

4. Animal experimentation has shown that correction of an inadequate intake of vitamin D results in the more economical utilization of calcium and phosphorus and also that the undesirable effects of improper ratios of calcium and phosphorus in the diet can largely be overcome by normal intake of vitamin D. The importance of these observations in their application to man is not entirely apparent because

of the lack of adequate clinical evidence showing the availability of different forms of calcium and phosphorus, but it may be stated that vitamin D has a favorable influence on calcium and phosphorus metabolism.

5. The vitamin D requirement appears to be greatest during the period of infancy. Beyond the age of infancy the exact vitamin D requirement of man under any specified conditions is not known but it appears that the requirement during pregnancy and lactation is increased.

6. Clinical evidence does not warrant the claim that massive doses of vitamin D are of benefit in chronic arthritis, in allergic disorders or in psoriasis.

MISUSE OF TERM VITAMIN F FOR LINOLEIC OR LINOLENIC ACIDS

In previous statements it has been pointed out that the use of the term vitamin F for linoleic or linolenic acids is not warranted. On recommendation of the Committee on Vitamin Nomenclature of the American Society of Biological Chemists, that organization and the American Institute of Nutrition have adopted the following statement:

> "The term 'Vitamin F' has been used in various ways in the past but recently has come into widespread use in promoting the sale of linseed oil and products alleged to contain so-called fatty acids. A group of biochemists interested in fat metabolism gave consideration to this matter during our last meeting. They informed this committee of the recommendation that the term vitamin F should not be used in referring to linoleic or linolenic acids, or so-called essential fatty acids. Your committee is in accord with these views, and it is recommended that the term vitamin F should not be used in referring to linoleic or linolenic acids, or any fatty acids or mixtures of fatty acids."

On recommendation of the Cooperative Committee on Vitamins, the Council on Pharmacy and Chemistry voted to endorse the action of the American Society of Biological Chemists and the American Institute of Nutrition.

VITAMIN K

The Cooperative Committee recommended to the Council that reports be made on the substance called vitamin K (one report was published in THE JOURNAL [Vitamin K: Its Properties, Distribution and Clinical Importance], April 15, 1939, page 1457).

POSSIBILITY OF REDUCING NUMBER OF TYPES OF VITAMIN A AND D PREPARATIONS FOR DIFFERENT CLASSES OF MANUFACTURED PRODUCTS

In following the action of the Council on dosages for vitamin A and D preparations it has become apparent that there are a great many types of preparations, making it almost a hopeless task for a physician to use these products to the best advantage, so far as dosage and potency are concerned. The suggestion was made to the Cooperative Committee that the number of types of these preparations be reduced by prescribing the potency for each type of product that might be accepted. There are very few preparations of the same type that have the same potency, whether it is cod liver oil, which ranges from 850 to 2,000 units of vitamin A and 85 to 250 units of vitamin D, or another oil of various constituents or the various concentrate preparations.

The committee recommended to the Council therefore that it consider in the near future the question of limiting arbitrarily the number of preparations as to strengths of vitamins A and D, and that the referees in charge of these products be instructed to bring in specific recommendations as to the types and potencies to be designated.

The proposal of the Pharmacopeia to designate three different types of vitamin containing oils was discussed. Criticisms were made of this proposal and it was decided that the subject of the nomenclature of these preparations should be brought to the attention of the U. S. P. Revision Committee in order that there might not be conflicts between the rules of the Council and the proposed names that might be adopted by the U. S. P. Revision Committee.

VITAMIN NOMENCLATURE

The question of vitamin nomenclature was again discussed. The members of the Cooperative Committee and of the Council have expressed the hope that those who discover in pure form the active principle of the vitamin or who discover new vitamins will follow some procedure whereby objectionable types of names will not be created. As has been pointed out previously, names which are therapeutically indicative or which use numbers, or the names of persons or towns, are not conducive to scientific nomenclature. The Council on Pharmacy and Chemistry has established contact with the Nomenclature Committee of the American Society of Biologic Chemists. This body has indicated willingness to consider proposed names in cooperation with the Council. The Council must insist that the names be not therapeutically suggestive.

II. Questions Primarily Concerning the Council on Foods

FORTIFICATION OF FOODS WITH VITAMINS

The idea of fortifying foods with dietary essentials is not new but had its beginning with the introduction of iodized salt. Later the question of the fortification of foods with vitamin D was brought up when the possibility of irradiation with ultraviolet or the addition of fish liver oil concentrates was developed commercially and the need for vitamin D in the prophylaxis of rickets was made evident. On the basis of evidence available, the Council on Foods decided that of the common foods only milk should be accepted when fortified with vitamin D. Other items such as chewing gum, beer, cake flour, candy, ice cream and sausage represent specific instances of indiscriminate fortification not recognized by the Council as being in the interest of public health.

As a result of its experience, the Council on Foods in 1936 adopted a statement of general policy regarding this question. It was then decided that general and indiscriminate fortification of foods with vitamins (as well as minerals) should be discouraged; the Council is aware, of course, that when a need is recognized for a certain dietary essential, and a food is shown to be suitable as a vehicle for that vitamin or mineral, fortification might be justified. New evidence and new problems would necessitate a reconsideration of the problems and policies.

Among the recent questions presented to the Council on Foods, reviewed by the Cooperative Committee, have been the following:

(*a*) Is oleomargarine fortified with vitamin A acceptable? This already has been decided in the affirmative because oleomargarine is used as an alternate for butter and it is desirable to provide in other food fats the vitamin A which is lost from the diet by the use of food fats lacking this vitamin.

(*b*) Should the fortification of flavored milk drinks with vitamin D be recognized? The Council has decided that products which are used like milk and which provide the calcium and phosphorus of milk in suitable amounts may well be fortified with vitamin D.

(*c*) What attitude should be taken toward food products fortified with preparations obtained from fish liver oils which provide both vitamins A and D? Some oleomargarines to which vitamin A has been added also supply a considerable amount of vitamin D, because both vitamins are present in fish liver oils. Similarly, some milk preparations to which concentrates of cod liver oil have been added as a source of vitamin D also supply additional vitamin A. The Committee agreed that no objection be taken to the concurrent presence of either vitamins A or D when preparations containing both vitamins are used for purposes of fortification with one, but the claims should be restricted to those supported by suitable evidence.

(*d*) The Council believes that fortification of cereal products with vitamin D is inadvisable because cereals ordinarily do not contain vitamin D and because this vitamin is of no value unless calcium salts also are provided. There are many phases of this question which require consideration and a more detailed report will be prepared on this subject. The Cooperative Committee reaffirmed the policy of the Council.

(*e*) What policy should be adopted in regard to the addition of vitamin B_1 to cereal products? The Council has taken no objection to the addition to cereal products of wheat germ or

dried yeast as sources of the vitamin B complex. Various considerations render unpractical the addition of wheat germ or dried yeast to many foods. Synthetic thiamin chloride is now available commercially and it has been suggested that milled cereal products might well have the vitamin B_1 content restored to the B_1 value of whole grain. This question involves many important points which need separate discussion.

(*f*) Ordinarily yeast is considered to be an important source of vitamin B_1 and vitamin G as well as other factors usually designated by the term "vitamin B complex." Fresh yeast is ordinarily not as rich a source of vitamin B_1 and vitamin G as has been supposed. The growing of yeast on culture mediums which will enhance the natural vitamin potency of the yeast, as well as other steps designed to accomplish the same end, represents a distinct advantage.

(*g*) The question has been raised whether it would be desirable to add vitamin B_1 to soda pop and whisky. The Council is opposed to such fortification because these preparations are not desirable in any nutritional program and because other considerations should make it self evident that fortification of alcoholic beverages cannot receive the approbation of the Council.

(*h*) The opinion of the Council regarding the addition of vitamin B_1 to sugars has been requested. There naturally are numerous questions which enter into any decision that might be made on this problem. A decision was withheld pending the accumulation of more data.

(*i*) Canned tomato juice usually contains about 40 per cent of the vitamin C content of fresh orange juice. One firm has asked the Council's opinion about the addition of vitamin C to canned tomato juice in order to increase the antiscorbutic potency to that of fresh orange juice. It was decided by the Cooperative Committee that the addition of vitamin C to canned tomato juice would serve no useful purpose because ordinary tomato juice when properly packed is a rich source of vitamin C and because there is no evidence of a need for a fortified product by the general public. The Council adopted the policy of not accepting at present canned tomato juice when fortified with vitamin C.

In discussing the subject there were many points to which consideration was given by the Cooperative Committee. The fortification of foods should make it easier for people generally to obtain an optimal diet. The vitamins of known significance in human nutrition are vitamins A, B_1 (thiamin chloride), C (ascorbic acid), D, G (riboflavin), nicotinic acid and possibly vitamin B_6. For these essentials the requirements are still under investigation and certainly the optimal quantities of any are far from being established. There are, however, certain more or less empirical rules that have been adopted as guides for the selection of dietaries which are considered suitable in the light of existing knowledge. It is becoming apparent that for various reasons, especially lack of knowledge, the people of the United States do not select foods to furnish the best possible diets for the money invested. More data are needed to determine actual intakes, but even with the data now available it is possible to point to some general tendencies toward deficiency in the national dietary. There is increasing evidence, for example, that more vitamin B_1 in the diet may be desirable. Although recent information shows that some meats, a hitherto unexpected source, provide considerable amounts of vitamin B_1, it also has been shown that many whole grain products of the ready-to-eat cereal class have lost much of the vitamin B_1 which was present in the original form, owing to the heating to which the products are subjected. There may be a need for more vitamin B_1 in the diet, but there is also a need for reexamination of available sources and greater emphasis in educational programs on the need for this vitamin. In any case present progress in teaching the applications of nutritional research to the public is slow because of few agencies devoted to this kind of education.

There is evidence that in certain parts of the country there is, in general, a low intake of other members of the vitamin B complex, particularly nicotinic acid and riboflavin. It is not established that marked deficiency of vitamin A and vitamin C in the diet occurs, but it is considered that the optimal diet requires more vitamin A and vitamin C than the average diet provides.

The fortification of foods with vitamins (or minerals) should not be viewed as a substitute for educational programs. Rather it should be considered that fortified foods simply afford an additional source of important dietary essentials needed for the attainment of optimal nutrition. Further, if vitamin A is to be made available in the form of fortified foods, such fortification may well be limited to food fats. Similarly, if vitamin B_1 is to be added to foods, those products which naturally furnish this vitamin but have lost it in processing should be the foods selected for its restoration. The addition of vitamin B_1 to milled cereal products thus appears to be justifiable.

It was brought out that it is important to keep the rules for dietary programs as simple as possible. If a great variety of vitamin D fortified foods are offered, for example, to the public, there is quite likely to be confusion in the mind of the mother trying to give her children the advantages of the modern knowledge of nutrition. This is an additional reason for recognition of milk alone of ordinary foods for fortification with vitamin D.

It was emphasized also that dietary deficiencies, while not limited to any group, are most likely to appear among people with low incomes. Any campaign for the nutritional improvement of foods should give careful consideration to the costs involved, because a higher cost of the final product may defeat the purpose of the fortification.

It was brought out that the fortification of foods cannot be considered without study of laws and regulations pertaining to foods. Thus, many municipalities have regulations prohibiting the addition of foreign substances to milk. In some localities this regulation, which obviously was formulated with a desire to protect the public, has been used to prohibit the addition of vitamin D preparations to milk. This action, in the opinion of the Council on Foods, is not in harmony with the modern knowledge of nutrition.

Another case in point is the prohibition by the Bureau of Animal Industry of the addition of oils containing vitamin A to oleomargarines made from animal fats. In this country animal products for human consumption are manufactured in establishments which are inspected by the Bureau of Animal Industry of the United States Department of Agriculture. That bureau has ruled that vitamin preparations come under the class of possibly harmful and deleterious substances and cannot be permitted on the premises of the manufacturing establishments. There is today no oleomargarine made from animal fats in the United States which contains added vitamin A, and under the present regrettable decision there can be none. Oleomargarines made from vegetable fats and oils may contain added vitamin A in the form of a small amount of a fish liver oil because these products do not come under the jurisdiction of the Bureau of Animal Industry. It may be mentioned that in some European countries no oleomargarine may be sold unless it is fortified with vitamin A and also with vitamin D.

In the opinion of the Council, legislation and regulations pertaining to foods should be enacted with reference to the best interest of the public. Fortification should not be prohibited but it should be controlled.

It was brought out that the policies regarding fortification of foods should be established with careful consideration of the known facts regarding the interrelationships of dietary essentials in the food product during storage and during digestion and metabolism. Thus, the addition of iron in large quantities may result in the catalytic destruction by oxidation of some of the vitamin values of foods. The addition of large quantities of phosphate may result in the loss of iron and calcium because of the formation in the digestive tract of insoluble phosphates of these minerals. It is also possible that some factors may have a harmful effect when too much is taken. Before nicotinic acid could be added to foods as part of the effort to prevent the incidence of pellagra, it would be necessary to know more about requirements and the behavior of this vitamin when added to foods. More information is needed about the interrelationship of vitamins and minerals in metabolism. These questions are amenable to experimental proof. There should be evidence of the merits of any fortified

food product before it is marketed. Fortification of foods must be guided by nutritional principles rather than the desire for developing new advertising claims.

On the basis of the foregoing discussion, the Cooperative Committee adopted the following resolutions regarding future policies for consideration by the Council on Foods:

I. *Resolved*, That the restorative addition of vitamins or minerals, in such amounts as will raise the vitamin or mineral contents of foods to recognized high natural levels, be encouraged; with the provision that such additions are to be limited to vitamins or minerals for which a wider distribution is considered to be in the interest of the public health, and with the further provision that the additions are made only to foods which naturally are principal sources of supply of the vitamins or minerals in question.

II. *Resolved*, That the indiscriminate fortification of foods with vitamins or minerals be discouraged. By such fortification is meant either the addition of any vitamin or mineral to foods which naturally are not principal sources of supply of the substance added, or the addition to a food of an amount of any vitamin or mineral which is larger than that naturally contained in some food of its class. The following exceptions will be recognized: 1. The addition of vitamin D to milk to an extent not to exceed 400 units per quart. 2. The addition of vitamin A to food fats, to an extent not to exceed the amount of vitamin A in butter with high natural content of vitamin A. In both cases, when the added vitamin is obtained from a natural source no objection will be made if it carries with it one or more other vitamins. 3. The addition of iodine to table salt in an amount not to exceed one part sodium or potassium iodide per 5,000 parts salt. It is recognized that all three of these exceptions represent restorative additions of vitamins or minerals, as defined in resolution I.

The foregoing resolutions were adopted in principle by the Council on Foods, further details to be developed later. It also was decided that steps should be taken to acquaint the public and the medical profession with the Council's opinion that natural foods are to be preferred and that any foods restored with vitamins or minerals in accordance with the foregoing principles likewise are to be preferred over foods processed in a manner resulting in a loss of the dietary essentials which they might be expected to supply.

CLAIMS FOR FOOD PRODUCTS RICH IN CERTAIN VITAMINS

Discussion was made of the claims that could be recognized for wheat germ, yeast products and dried cereal grasses, all of which are considered as special purpose foods. The usefulness of these products is demonstrable by chemical analysis and biologic assay, together with a knowledge of the nutritional requirements for the various dietary essentials. Nutritional claims for these products should not exceed those recognized for the vitamins and other dietary essentials which they contain, due consideration being given to the amounts supplied by the portion, or dosage, which may be used daily.

VITAMIN MIXTURES

There have been developed by the industry numerous fabricated mixtures of vitamin preparations, which are marketed in the form of capsules. These contain usually preparations made from fish liver oils, supplying vitamins A and D, and extracts of yeast or other sources of vitamin B_1 and riboflavin. Sometimes vitamin C is included, although not many commercial preparations contain this factor. The field is not limited to capsules, but there is also a compressed yeast fortified with carotene and providing vitamin D and there are various tablets which likewise are sold to the public as vitamin preparations of relatively high potency.

These vitamin mixtures may be a commercial success, but they cannot replace the need for adequate amounts of a well balanced diet. Vitamin mixtures may have some reason behind the selection of vitamins which they contain and the amounts of each that are present, but if so, the reason is a "trade secret" which has not been divulged. Certainly there is no rational basis for placing in capsules amounts of vitamins A and D which, in the amounts recommended by the firms, are several times a therapeutic dose, and amounts of vitamin B_1 and riboflavin which are almost insignificant compared to the contribution which an adequate diet would supply. Advertising campaigns and other efforts to promote the indiscriminate use of expensive polyvitamin mixtures are unfortunate because the "educational" program is not based on sound principles of nutrition or medicine. It is not denied that there may be a limited field in which polyvitamin mixtures might be useful, if the qualitative and quantitative composition of the mixtures were scientifically rational. It is conceivable, for example, that a physician might desire to provide a patient on a restricted therapeutic diet with vitamins which ordinarily are supplied by an adequate diet. But the available preparations of vitamin mixtures obviously cannot solve the problem of giving a patient the vitamins and food which he needs. The use of vitamin mixtures by the public is no assurance of "good health"; their daily use is no guaranty that all of the vitamins which a person must secure will be provided.

The Committee reaffirmed the policy of the Council on Pharmacy and Chemistry not to accept irrational fabricated mixtures of vitamins. The two councils concurred.

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

ANTIPNEUMOCOCCIC SERUM, TYPE I (See New and Nonofficial Remedies, 1939, p. 406).

Lederle Laboratories, Inc., Pearl River, N. Y.

Refined and Concentrated Antipneumococcic Serum, Type I-Lederle.—Also marketed in packages of one vial containing 20,000 units and one vial containing 50,000 units.

ANTIPNEUMOCOCCIC SERUM, TYPE II (See New and Nonofficial Remedies, 1939, p. 407).

Lederle Laboratories, Inc., Pearl River, N. Y.

Antipneumococcic Serum, Refined and Concentrated, Type II.—Also marketed in packages of one vial containing 20,000 units and one vial containing 50,000 units.

ANTIPNEUMOCOCCIC SERUM, TYPES I AND II COMBINED (See New and Nonofficial Remedies, 1939, p. 409).

Lederle Laboratories, Inc., Pearl River, N. Y.

Bivalent Antipneumococcic Serum, Refined and Concentrated.—Also marketed in packages of one vial containing 20,000 units and one vial containing 50,000 units.

ANTIPNEUMOCOCCUS SERUM, TYPES IV AND VIII COMBINED (See New and Nonofficial Remedies, 1939, p. 411).

Lederle Laboratories, Inc., Pearl River, N. Y.

Antipneumococcic Serum, Types IV and VIII, Refined and Concentrated.—Also marketed in packages of one vial containing 50,000 units.

ANTIPNEUMOCOCCUS SERUM, TYPES V AND VII COMBINED (See New and Nonofficial Remedies, 1939, p. 411).

Lederle Laboratories, Inc., Pearl River, N. Y.

Antipneumococcic Serum, Types V and VII, Refined and Concentrated.—Also marketed in packages of one vial containing 50,000 units.

TETANUS TOXOID, ALUM PRECIPITATED (See New and Nonofficial Remedies, 1939, p. 436).

Gilliland Laboratories, Inc., Marietta, Pa.

Tetanus Toxoid, Alum Precipitated (Refined)-Gilliland.—Marketed in packages of two 1 cc. and two 0.5 cc. vials each containing one immunization treatment and in packages of one 10 cc. vial and one 5 cc. vial each containing five immunization treatments.

CAFFEINE WITH SODIUM BENZOATE (See New and Nonofficial Remedies, 1939, p. 154).

Ampuls Caffeine with Sodium Benzoate, 2 cc.: Each 2 cc. contains in sterile aqueous solution caffeine with sodium benzoate U. S. P. 0.5 Gm. (7½ grains).

Prepared by the Wm. S. Merrell Company, Cincinnati.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

535 North Dearborn Street - - - Chicago, Ill.

Cable Address - - - - "Medic, Chicago"

Subscription price - - - - - Eight dollars per annum in advance

Please send in promptly notice of change of address, giving both old and new; always state whether the change is temporary or permanent. Such notice should mention all journals received from this office. Important information regarding contributions will be found on second advertising page following reading matter.

SATURDAY, AUGUST 12, 1939

METABOLIC CHARACTERISTICS OF CANCEROUS TISSUE

The first significant advance in the study of the metabolism of tumors was made by Warburg,[1] who developed evidence of an altered carbohydrate metabolism of tumors. Thus was shown the ability of tumors to ferment aerobically from 90 to 95 per cent of available dextrose with the formation of lactic acid instead of oxidizing the carbohydrate to carbon dioxide and water as in normal tissue metabolism. This abnormal type of metabolism is not limited to malignant tissue, however. It has been found to be characteristic of all fast growing tissues. Kögl and Erxleben[2] have recently reported that several amino acids in malignant tissues occur as the unnatural stereo-isomers. While the significance of this remarkable fact cannot now be adequately evaluated, it is the first definite evidence of a qualitative difference in the metabolism of normal and malignant tissues.

An analysis of the protein hydrolysates of four malignant tumors indicated that as much as 42 per cent of the glutamic acid was present in the unnatural dextrorotatory form. Lysine and leucine were also found as their unnatural stereo-isomers in smaller quantities. Similar hydrolysis of normal tissue yielded only the natural levorotatory forms of these amino acids. Since the enzyme system involved in the synthesis and degradation of each of the optically active isomers is highly specific, the presence of the unnatural forms would indicate that the particular tumor enzymes needed to metabolize these amino acids are less specific or are present in forms not native to normal tissue. The synthesis of protein, which is represented in the tumor by its rapid growth, is a result of the coordinating action of these different proteolytic enzymes; such a marked qualitative difference in behavior might greatly alter the rate of growth or regression (lysis) of the tumor.

In view of the important role which recent progress in biochemistry has given to glutamic acid in linking intermediary carbohydrate metabolism with protein metabolism, the results reported by Kögl and Erxleben are of special importance. Euler and his co-workers[3] have separated from normal liver tissue a specific enzyme which, when supplemented with the oxidized form of coenzyme (dehydrocozymase), dehydrogenated glutamic acid, while, in the presence of the reduced form of the coenzyme, the enzyme synthesized glutamic acid from ammonia and α-ketoglutaric acid, which is a product of carbohydrate metabolism. Only the normal levorotatory form of glutamic acid is dehydrogenated by this enzyme from normal liver.

Braunstein and Kritzmann[4] have further shown the importance of glutamic acid as a key substance in tissue metabolism by experiments in which the enzyme system of tissues was able to transfer the amino group from certain amino acids to α-ketoglutaric acid with the formation of glutamic acid, or reverse this transfer. While these authors found this transaminating enzyme system in all tissues except tumor tissue or nucleated red blood cells, Euler reports that it is present in tumor tissue but in smaller amounts than in muscle tissue.

The intensive investigations of tissue metabolism are constantly yielding new knowledge concerning the enzymic activities of normal and malignant tissues. If the observations of Kögl and Erxleben can be confirmed by other workers and it is found that all types of malignant tissues contain the unnatural forms of amino acids, a new and fertile field for study into the nature of cancer will be opened.

1. Warburg, Otto: Ueber den Stoffwechsel der Tumoren, Berlin, Julius Springer, 1926.
2. Kögl, Fritz, and Erxleben, Hanni: Ztschr. f. physiol. Chem. **258**: 57 (Nos. 2 and 3) 1939.
3. von Euler, Hans; Adler, Erich; Günther, Gunnar, and Das, Nalin Bandhu: Ztschr. f. physiol. Chem. **264**: 61 (No. 2) 1938.
4. Braunstein, A. E., and Kritzmann, M. G.: Nature **140**: 503, 1937. Enzymologia **2**: 129, 1937.

LISTERINE AND ALKA-SELTZER—THE FEDERAL TRADE COMMISSION TAKES ACTION

Some of the most interesting folklore in the development of American advertising—legends long accepted by many popular periodicals and by many people—is about to pass into the limbo of forgotten things. The Wheeler-Lea legislation seems to be functioning.

On August 3 the Federal Trade Commission entered into a stipulation with the Lambert Pharmacal Company of St. Louis, manufacturer of "Listerine Antiseptic," to cease and desist from "representing, by direct statement or by inference, that all dandruff is due to an infection with Pityrosporon ovale or any other organism; that dandruff necessarily is a germ disease; that the dandruff germ has been isolated or identified; that the presence of Pityrosporon ovale necessarily means dandruff or that with its destruction dandruff disappears; that dandruff is necessarily infectious, contagious or 'catching' or is in all instances passed from one person to another, or that any of the foregoing

assertions have been proven by findings of scientists or otherwise, or is a 'scientific fact' or a 'fact definitely established by scientists.'"

The Federal Trade Commission said, moreover, "that it is also stipulated that the respondent desist from representing that the product either cures or permanently relieves dandruff; that the product 'kills the dandruff germ,' 'attacks the cause of dandruff,' 'or gets at the cause' or 'at the root of the trouble' or penetrates infected hair follicles or 'annihilates' the dandruff germ; that the product frees the scalp and hair follicles of the parasite that saps their vitality or 'spreads a germ-killing film over the scalp'; that the product has 'marked curative properties due to certain ingredients in a unique combination shared by no other antiseptic'; that ordinary remedies 'aren't even antiseptic,' are 'smelly,' affect only surface symptoms, or merely remove surface symptoms temporarily, or that competitive products are obviously inferior to 'Listerine Antiseptic' as a remedy for dandruff—when such are not the facts."

The so-called research on which the claims of the manufacturer for this alleged virtue of listerine were based had never been accepted by competent dermatologists as authoritative; certainly there was not the slightest controlled evidence to indicate that listerine or any similar combination could have such virtue in controlling dandruff. Thus this product, which is essentially a formula like the liquor antisepticus of the National Formulary, will return to its original claims in relation to overcoming halitosis.

The history of the advertising of listerine as a preventive of halitosis has been told on many occasions. It laid the basis for many a vast advertising campaign associated with diseases discovered by advertising geniuses who thumbed the medical dictionaries. Out of the announcements of halitosis came such emphasis as has been placed on acidosis, athlete's foot, dyskinesia and similar conditions. The halitosis campaign reached its apotheosis with the advertisement which announced that "She Built Her Bridge Table Two Feet Wider." Obviously her breath could be detected two feet away but not four feet from her. Then she tried listerine and didn't have to stretch any more for the cards in the dummy.

The second decision of the Federal Trade Commission, dated August 6, involved a stipulation of the Miles Laboratories, Inc., Elkhart, Ind., with the Federal Trade Commission to discontinue misleading representation in the sale and distribution of Alka-Seltzer. This product is essentially a mixture of sodium acetylsalicylic acid with baking soda, and citric acid. Every one is familiar with the claims that have been made for the product over the radio and in other advertising.

Now the respondent company agrees "to cease the use of advertising matter implying that colds, neuralgia, distress after meals, and 'common everyday ailments' result from excess acidity of the blood, an acid condition of the blood, or deficient alkaline reserve of the blood, and that alkalinizing effect of 'Alka-Seltzer,' by correcting such acid condition or restoring the alkaline reserve, will be a proper treatment for the ailments mentioned."

The respondent further agreed "to discontinue representations implying that headaches, upset stomach, and aches and pains result from, or are associated with, excess acidity of the blood, an acid condition of the blood, or a deficiency in the alkaline reserve of the blood, except when the ailments mentioned may be shown by competent scientific evidence to be directly associated with such conditions of the blood, and subject to this exception, to cease making representations implying that the taking of 'Alka-Seltzer,' by correcting the acid condition of the blood or restoring its alkaline reserve, will be a proper treatment for such ailments."

The respondent also stipulated "that it would cease representing that other therapeutic effects of 'Alka-Seltzer' exceed the recognized benefits to be derived from neutralization of hyperacidity of the gastric contents or the analgesic and other effects of sodium acetylsalicylate together with the action of buffer salts."

According to an examination of the product in 1932, persons who follow the directions to dissolve two tablets of alka-seltzer in a glass of water get nearly 9 grains of aspirin and nearly 1 grain of salicylic acid with their mixture of citric acid and baking soda. Those who do as suggested and take sixteen such tablets a day get over 70 grains of aspirin and 6 grains of salicylic acid in twenty-four hours. Whether or not the formula has been changed since that time is not known.

It will be interesting to see what the Miles Laboratories, Inc., find to talk about now that the government has told them what they cannot say. Perhaps they will decide to tell the people that what they are offering is essentially an effervescent tablet of aspirin.

THE NATIONAL HEALTH PROGRAM

The Seventy-Sixth Congress adjourned sine die August 5 without acting on the Wagner Health Bill, S. 1620. The Senate Committee on Education and Labor, however, submitted a preliminary report [1] August 4 and announced its intention to submit a definite report soon after the next session of Congress convenes. The subcommittee which has the bill under its immediate consideration plans to report an amended bill. The committee expresses the opinion that federal legislation along the general lines of the Wagner Health Bill is necessary to strengthen the health services of the nation and to make provision for progressive and effective improvement of health conditions in all parts of the country and among all groups of people. The committee was not convinced that the enactment of the bill would bring about revolutionary or dangerous changes in the established methods of medical service.

Congress passed in the last hours of the session just ended an act to amend the Social Security Act, and for other purposes, H. R. 6635, which covers primarily

1. Senate Report No. 1139, 76th Congress, 1st Session.

changes in the economic provisions of the act. In the Senate, certain amendments were added, later accepted by the House, largely increasing the amounts authorized to be appropriated for grants to states for maternal and child welfare, under the supervision and control of the Children's Bureau, and for public health work under the supervision and control of the Public Health Service. An amendment adopted by the Senate, proposing the establishment of an advisory council on disability insurance by the Committee on Finance of the Senate and the Committee on Ways and Means of the House of Representatives, in cooperation with the Social Security Board, was eliminated in conference.

On August 4, Senator Lodge of Massachusetts introduced a bill to provide health insurance to certain workers in severe economic distress, S. 2963. The bill proposes to provide certain limited medical and hospital services by physicians and hospitals chosen by the beneficiaries, but its benefits are to be limited to unemployed persons in need of medical and hospital services who during their periods of employment paid not less than certain stated amounts as taxes under the provisions of the Social Security Act. The bill was referred to the Senate Committee on Finance. Obviously it cannot be called up for consideration until Congress again convenes.

Current Comment

SCIENTIFIC AND COMMERCIAL CONSIDERATION OF VITAMINS

In this issue (page 589) appears a report by the Cooperative Committee on Vitamins of the Council on Pharmacy and Chemistry and the Council on Foods. The report, which is admirably succinct, is divided into two parts, one concerning vitamins as drugs and one dealing with vitamins as foods. The Council on Pharmacy and Chemistry again summarizes permissible claims for the use of vitamins in the prevention and treatment of disease. The report endorses the elimination by the American Society of Biological Chemists and the American Institute of Nutrition of the term "vitamin F"; this has not been established as a vitamin and has been commercialized by firms which have marketed cosmetics containing unsaturated fatty acids with the claim that these were "vitamin F." The Council recognizes the desirability of reducing the number of types of vitamin A and D preparations in different classes of manufactured products. There is certainly no necessity for the tremendous number of products, which vary from one another chiefly in the relative amounts of active ingredients, vitamins A and D, which they contain. The problems of the Council on Foods are complicated by the current tendency toward fortification of foods with excess of vitamins; some of this fortification is based on common sense but often there is no apparent basis except the desire to develop a product that can be sold. In general the Council on Foods feels that reconstruction of foods by the addition of vitamins lost in manufacturing processes is justified, but mere fortification for the sake of fortification the Council cannot commend. The councils condemn heartily the needless, irrational and unscientific combinations of vitamins for treatment of diseases or for the alleged easy attainment of superabundant well being. This is the third report of the Council on Pharmacy and Chemistry in recent years on the status of vitamins; it indicates how rapidly research with vitamins and their clinical application move forward. Within the last few months vitamin B_6 has been synthesized, the chemistry of vitamin K has been clarified to a considerable extent, and evidence has accumulated about the significance of these factors and of riboflavin in human nutrition.

CORONARY OCCLUSION IN PHILADELPHIA

Hedley[1] has recently analyzed 5,116 deaths in the five year period ended Dec. 31, 1937, reported by the medical profession of Philadelphia as due to acute coronary occlusion. During this period the total mortality attributed to this cause increased more than 125 per cent in Philadelphia. In spite of the great increase in the number of deaths from coronary occlusion, however, the age distribution by decades and the mean age at death remain practically the same for all the years in the period under study. Hence it is concluded that the increase in deaths from acute coronary occlusion cannot be attributed to a tendency to report deaths among the very old as due to this cause. The ratio of males to females was approximately two to one. The mean age at death among all cases was 61.2 years. Further, the mean age at death and age distribution by age decades indicated that deaths among white females occurred at considerably older ages than among white males. Although acute coronary occlusion occurs less frequently among Negroes than among white persons, deaths from this cause among Negroes occur several years earlier. The mortality from this cause appears to be somewhat higher among the Jews than among white Gentiles. However, Hedley points out that this may be due to the large number of Russian Jews and may not prevail among native-born Jews. There was no definite seasonal variation of deaths from acute coronary occlusion as judged by the monthly distribution of deaths, although there were considerably fewer deaths during the warm months. The mortality rate among white persons increased from 36 per hundred thousand of population in 1933 to 84 in 1937. Among Negroes the increase was only from 25 to 27. The increase in reported mortality from acute coronary occlusion during this period cannot be attributed, Hedley says, to any great extent to the aging of the population in general or to the aging of the foreign born population in particular. Improvement in diagnosis was probably the main reason for the increase. In fact, the diagnosis of coronary occlusion cannot even yet be regarded as stabilized. Some further difficulties can be anticipated therefore in determining whether subsequent possible increases in the incidence of mortality from acute coronary occlusion are real or apparent.

1. Hedley, O. F.: Analysis of 5,116 Deaths Reported as Due to Acute Coronary Occlusion in Philadelphia, 1933-1937, Pub. Healt' Rep. 54: 972 (June 9) 1939.

ORGANIZATION SECTION

GRADUATE MEDICAL EDUCATION

A PROGRESS REPORT OF THE FIELD STUDY ON GRADUATE MEDICAL EDUCATION IN THE UNITED STATES BEING CONDUCTED BY THE COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

NEW MEXICO

In 1937 the New Mexico Medical Society Committee on Maternal and Child Health, which is composed of an obstetrician and a pediatrician and the secretary of the state society, advised the director of the Division of Maternal and Child Health of the New Mexico Department of Public Health regarding postgraduate instruction in obstetrics. At the request of the director, district health officers proposed postgraduate courses to members of various county medical societies throughout the state. In May 1938 physicians in two counties requested instruction, and an out of state obstetrician gave three lectures in each place. Twenty-two of the thirty-eight physicians in the two localities attended. No registration fees were charged, since federal funds were used. In September 1938 six other county medical societies were provided with instruction by another out of state obstetrician, who gave five two hour lectures in each county. Approximately seventy-nine of 141 physicians in these sections registered.

In May 1939 three county societies again requested the lecture courses in obstetrics, and one of the out of state obstetricians returned to New Mexico for the series. Movies were utilized and the instructor was available for consultations.

There are 419 licensed physicians in the state, of whom 256 are members of the New Mexico Medical Society.

TEXAS

ORGANIZATION AND ADMINISTRATION

The opinion has been expressed that in Texas postgraduate instruction may best be presented in medical centers of the state, their teaching facilities being utilized to advantage. Itinerant postgraduate courses would be difficult to organize to provide satisfactory programs in a state with sparsely settled areas and with varying geographic and climatic conditions. With these principles in mind, a postgraduate program in obstetrics and pediatrics for each of the fifteen councilor districts of the state was proposed in 1936 by members of the State Medical Association of Texas and of the Division of Maternal and Child Health of the Texas State Department of Health. The committee on maternal and child health of the state association, composed of ten practicing physicians, pediatricians and obstetricians with Dr. C. R. Hannah as chairman, and representatives of the state department of health provided the necessary machinery for the organization of postgraduate instruction.

INSTRUCTION IN OBSTETRICS AND PEDIATRICS

This committee in the succeeding two years sponsored the series of courses for physicians in thirty-nine communities and also provided a series of public health lectures. Instructors were chosen chiefly from the faculties of the two medical schools of the state and physicians in practice who were able to devote time to this effort. They arranged their own lectures to cover subjects outlined by the committee but worked under the direction of the state department of health. Honorariums and traveling expenses were paid instructors out of funds received by the department from the federal government.

The postgraduate medical instruction in obstetrics and pediatrics covered a period of not less than thirty hours given in three consecutive monthly programs of two days in each councilor district. Lectures, demonstrations and round table discussions were included. During the two years that the program of pediatrics and obstetrics was given, 1,291 practicing physicians received instruction. No registration fees were charged.

Each councilor district made its own provision for the conduct of courses in its respective locality. In each district a committee of three members with the councilor of the district as chairman had complete supervision of all postgraduate activities. County medical societies in turn appointed a local committee on arrangements, under the direction of the district committee.

The cooperation of the University of Texas School of Medicine, Galveston, and of the Baylor University College of Medicine, Dallas, the Texas State Dental Society, the Texas State Association of Obstetricians and Gynecologists and the Texas Pediatric Society was obtained in supporting this educational enterprise.

ACTIVITIES OF THE COMMITTEE ON POSTGRADUATE INSTRUCTION

In 1937 the committee on postgraduate instruction, with five members each appointed for one year, was formed by the state medical association. At that time the committee studied the postgraduate courses being given in Texas and the advisability of the state association adopting a similar program. The state association's ways and means committee had recommended that the association dues be raised $1 a year in order to carry on scientific work successfully. It was also suggested that clinical conferences similar to those being given each year in Dallas, San Antonio and Houston be conducted by the state association each fall.

In 1938 the postgraduate committee emphasized the need for full cooperation of medical organization, medical schools and hospitals in promoting postgraduate instruction. It was believed that there was a need in Texas for additional opportunities for postgraduate training. The committee was of the opinion that this should take the form of extension medical courses made available through the facilities of the state medical association, the medical schools and the hospitals and should be carried to the home communities of as many physicians as possible. The two additional phases of postgraduate medical instruction which it was thought should be sponsored by the state medical association were (1) reestablishment of courses in fundamental medicine given during the summer several years ago in the medical schools and (2) formation of a speakers' bureau in the state association to give extension courses in its constituent societies. In 1939 the proposals made by previous committees of postgraduate medical education were considered but at that time no additional recommendations were made.

CLINICAL CONFERENCES

Three clinical conferences are given at different times each year in three cities of Texas. These are the Dallas Southern Clinical Society, Dallas, the Postgraduate Medical Assembly of South Texas, Houston, and the International Postgraduate Medical Assembly, San Antonio. On alternate years in El Paso postgraduate meetings of the Southwestern Medical Association are held. The clinical society of Dallas is an independent medical organization. The Houston society is sponsored by the three district societies of the state medical association and in San Antonio the postgraduate meeting is promoted by two district societies. Registration fees of $10 each in Houston and in Dallas and income from commercial exhibits support the programs. This fee entitles the registrant to all the activities during the three or four day session. In San Antonio, dues from members and income from exhibits aid in financing. A centrally located hotel is used in each locality. Lectures, clinics, symposiums, round table discussions and, in one case, clinical pathologic conferences are given. Subjects of general

and special interest are included. Out of state instructors are provided, and in San Antonio both in state and out of state physicians participate. Attendance each year varies from 650 to 800 physicians. Operative clinics are sometimes held.

In addition to the annual clinical conference of the Dallas Southern Clinical Society, an extension service is available for scientific programs in county and district medical societies throughout the state. This is offered throughout the year in every field of medicine. Topics for discussion are selected by the local societies either singularly or in symposiums.

The Dallas Southern Clinical Society was organized in 1929 through the auspices of the Dallas County Medical Society and the membership of the clinical society includes 150 physicians of Dallas. Each member is required to take part in the extension service or to participate regularly in some educational program. The Postgraduate Medical Assembly of South Texas was organized in 1932. Local physicians do not participate in the programs of this society. The International Postgraduate Medical Assembly of Southwest Texas was organized in 1933. Full time executive secretaries and offices are maintained by two of these sectional societies.

In addition to the four metropolitan areas referred to, councilor district societies in other sections of the state hold one or two day postgraduate meetings. These include small clinics of the Tarrant County Medical Society held at Fort Worth each year, the district meeting held in Mineral Wells and the district meeting held in Amarillo. The Tarrant County Medical Society gave its first program of postgraduate instruction in 1906. At that time there were twelve courses offered by its members. From five to fifteen hour periods were devoted to such courses as anatomy, pathology, bacteriology, physiology, pharmacology, clinical diagnosis, medical jurisprudence and the history of medicine. At present this society conducts a one day clinic each year in which four or five out of state physicians participate. The program extends through twelve hours of the day. Meetings are held in a local hotel and lectures are illustrated with movies. The district meeting at Mineral Wells is similarly organized. Registration fees of $1 are charged in each district and the attendance at each meeting varies from 200 to 300 physicians.

POSTGRADUATE ACTIVITIES IN MEDICAL SCHOOLS

Beginning in 1922 the University of Texas School of Medicine and the Baylor University College of Medicine cooperated with the committee on medical education and hospitals of the state medical association in organizing a postgraduate course of one week's duration each summer in the two institutions. These were review courses in general subjects of medicine. No registration fees were charged. The only expenses to physicians were cost of transportation and maintenance. Attendance averaged fifty annually in each institution. After two years, however, the courses were discontinued, since the faculties of the medical schools were not compensated for this type of instruction and had to forego periods usually devoted either to research or to vacation. This kind of instruction in teaching centers offered certain facilities that were not available to the same extent in other sections of the state.

OTHER POSTGRADUATE ACTIVITIES

The state medical association has offered a package medical library service to the physicians of Texas since November 1931. The library consists of a collection of more than 90,000 reprints and ten years open files of 160 periodicals in addition to more than 4,300 volumes available for mailing to members of the association. Unbound files of medical journals are kept for ten year periods. The library requires the services of one full time and one part time librarian. Twenty-five cents is charged each member requesting a library package.

INSTRUCTION OF NEGRO PHYSICIANS

Postgraduate instruction was first offered to the Negro physicians of Texas at Prairie View State College, Prairie View, in March 1937. This three day course of lectures and demonstrations was given under the joint sponsorship of the Texas Tuberculosis Association, the Texas State Department of Health, the Julius Rosenwald Fund and the Lone Star State Medical, Dental and Pharmaceutical Association. Subjects included were obstetrics, pediatrics, venereal diseases and tuberculosis. Three out of state and seven Texas physicians gave the instruction. Fifty-seven practicing physicians registered for the course. In March 1938 the graduate assembly was repeated under the same auspices over a four day period. Four out of state and nine Texas physicians constituted the faculty. The use of clinical material was emphasized. A $1 registration fee was paid by the fifty-nine who enrolled. In March 1939 a third four day assembly was held. Six out of state and seven Texas physicians gave the instruction, for which seventy-two practicing physicians registered. Clinical material was used in the demonstrations. Preventive medicine, communicable disease and antepartum and postpartum care were emphasized.

In addition to attending the annual postgraduate assemblies, Negro physicians of Texas have been offered the opportunity of obtaining two weeks of instruction at the Kerrville State Sanatorium. Six physicians registered. The Texas State Department of Health and the Texas Tuberculosis Association are sponsoring this intramural course also.

Of the 6,795 physicians practicing in the state, 4,483 are members of the State Medical Association of Texas.

VIRGINIA

ORGANIZATION AND ADMINISTRATION

In 1927 Dr. J. W. Preston, president-elect of the Medical Society of Virginia and chairman of the society's special committee on postgraduate study, enlisted the assistance and cooperation of the extension department of the University of Virginia to make a survey of postgraduate instruction in other states and to outline a suitable plan for continuation instruction for practicing physicians of the state of Virginia. As a result of this study Dr. J. Allison Hodges, chairman of the committee on medical education and hospitals of the state society, outlined such a plan in October 1929, which was adopted. The plan provided for the annual election of seven members of the society, who would compose the department of clinical and medical education as follows: three members chosen from the society membership at large (one the president-elect for the year, as chairman), one representative from each of the two medical schools in the state, one representative from the state health department and an executive secretary—either a physician or a layman.

The dominant idea in the formation of this department was that it provide a central medium between the society and its constituent units and act as a continuing and correlating body in providing postgraduate education to the practicing physicians of the state. It would assist local societies in securing suitable lecturers and clinicians and otherwise cooperate on request. An advisory board composed of members of the society's standing committees on medical education and hospitals and on scientific work in clinics aided the department.

From the beginning the department of clinical and medical education has provided practicing physicians in their own communities with lectures and clinics in recent advances in medicine, surgery, obstetrics and pediatrics. The department has aided in the establishment of a fully organized postgraduate clinical course in each of the medical schools of the state. It has assisted the state society in the publication and distribution of announcements of all courses and has published the names of physicians who have enrolled for postgraduate instruction. The director and the associate director of the extension division of the University of Virginia have acted as executive agents for the department and have donated their services and the facilities of the division to the medical society. The department has also had the cooperation of Dr. Warren F. Draper, state commissioner of health, who was able to obtain financial support for the program.

The state medical society has made a financial contribution yearly and practicing physicians have paid fees of from $2.50 to $10 for each course. After the plan was under way, the Commonwealth Fund of New York aided financially. With the assurance of added financial support it was possible to employ a competent physician full time to act as field clinician. The cooperation of the field organizer from the extension division of the University of Virginia made it possible to enlist the active support of county medical societies.

Instruction in obstetrics and pediatrics was desired and at first these courses were emphasized. Since 1937 instruction in medicine has been attempted. Instructors for the postgraduate courses until recently have been clinicians devoting full time to this work. At present faculty members from medical schools of the state give most of the instruction. They are compensated with small honorariums and travel expenses. Whenever possible, an effort is made to have registration fees sufficient to cover this expense. Service necessary for organization and administration is donated by the University of Virginia.

During 1930-1931, clinical meetings were held in eight counties of the state. Mr. George W. Eutsler, executive secretary for the department of clinical and medical education and associate director of the extension division of the University of Virginia, was responsible for sending notices to physicians in these areas. He also notified physicians of the postgraduate clinics being held in the medical schools of the state.

The chairman of the department of clinical and medical education, Dr. James C. Flippin, was active in supplying speakers for the meetings of county medical societies throughout the state. A speakers' list was printed in the *Virginia Medical Monthly* and reprinted in pamphlet form for distribution to the officers of county societies.

In January 1931 a grant of $10,000 was obtained from the Commonwealth Fund and an appropriation of $2,500 was made by the Medical Society of Virginia to continue the program of instruction in antepartum and postpartum care.

INSTRUCTION IN OBSTETRICS, GYNECOLOGY AND PEDIATRICS

From May 1932 to September 1933 Dr. Maxwell E. Lapham, field clinician, completed thirty-three classes covering the entire southern section of the state. Classes were grouped in six circuits, the first five having five centers each and the last having six. The registration at these short courses of two weeks' duration was 421. Two hundred and sixty-nine consultations were held and 184 patients were demonstrated in clinics.

Twenty-three classes were conducted during 1933-1934. Two hundred and twenty-nine physicians enrolled. There were 282 consultations with the field clinician, and 107 patients were demonstrated in the clinics. The tenth circuit, which included five towns, was completed in 1934-1935. Thirty-six physicians enrolled. Also during this year an out of state pediatrician directed a series of ten two hour lectures and demonstrations in two sections of the state. Twenty-eight attended one section and sixteen the other.

The general plan for this postgraduate instruction was to conduct lecture-clinics, having meetings of two hours' duration once a week for ten weeks in each locality. Every county medical society was given an opportunity to have the course. Usually the clinician lectured for one hour and then conducted a clinic or held an informal discussion during the second. On the day of the meetings he was available for professional conferences and bedside consultations. The first year the programs were held in the larger cities and towns of the state and the second year in the smaller towns and rural sections. Actually the percentage of physicians within reach of the clinics during the second year was higher than in the first.

During 1935-1936 the graduate program was less active partly because of insufficient financial support. Clinics were conducted by two out of state pediatricians in four sections of the state. With the aid of the state department of health, one full time instructor in obstetrics and one in pediatrics were employed to organize clinics and to continue the educational program of the state medical society, and the next year these field clinicians, together with members of the faculties of the two medical schools in Virginia, comprised the teaching staff for carrying on the postgraduate instruction.

There were ten circuits, which included thirty-three centers in which lecture-clinics were held in the subjects of obstetrics and gynecology. These courses reached physicians in forty-four counties of the state. The total attendance was 749. In addition, 178 consultations were held. Nine circuits in pediatrics included twenty-two centers accessible to physicians in twenty-nine counties. The total attendance was 972, and there were 476 consultations with physicians.

Postgraduate instruction in obstetrics and gynecology was completed during 1937-1938, it having been offered in every community of the state. Thirty-four counties were included that year with a total attendance of 957. One hundred and ninety consultations were held. The pediatric lecture-clinics were continued in thirty-four of the 100 counties in the state. The total attendance was 751, and 306 consultations were held.

OTHER TYPES OF INSTRUCTION

In cooperation with the department of clinical and medical education of the state medical society, two postgraduate clinics were held each year at the University of Virginia Hospital. These were given usually by members of the faculty of the department of medicine.

In 1936-1937 two postgraduate clinics were held by the department of medicine of the University of Virginia, forty-five practicing physicians attending one and 103 the other. Out of state physicians participated in this intramural instruction.

A short course in internal medicine was given in the eastern part of Virginia by local medical societies during 1937-1938. Twenty-eight physicians attended. The Medical College of Virginia provided instructors. Two other medical societies of the state conducted postgraduate instruction on a regional or county basis. The number of physicians attending the postgraduate clinics held by the University of Virginia Department of Medicine in 1937-1938 was 164.

A postgraduate course in internal medicine is now available to any county society of the state which requests this instruction. In 1938-1939, faculty members of the two medical schools have given courses with from three to six sessions in each of seven counties. These consist of lecture-clinics and round table discussions. In one county there was a total of ten weekly meetings. Registration fees vary from $5 to $10. Subjects for discussion are chosen by the physicians in each locality.

During 1938-1939 there was a symposium on the endocrines at the University of Virginia and a postgraduate clinic on general medical subjects. Eighty-one practicing physcians attended the first and fifty-nine the second session. A prominent out of state medical school instructor participated in each program. A symposium on vitamins was held in May 1939 in which three out of state physicians took part. Seventy-two practicing physicians registered for this day of graduate clinics.

Each year since 1930 the Medical College of Virginia has held an annual Stuart McGuire Lecture. From one to eight out of state physicians participate in this lectureship. In 1939 the lecture series was combined with postgraduate clinics and was devoted to a symposium on psychiatry. Lectures, discussions and demonstrations comprised the two day program. There was no registration fee. From thirty to fifty practicing physicians from Virginia attend these annual sessions.

The names of physicians who attend courses of instruction given by the state medical society appear in a special section of the *Virginia Medical Monthly*.

Courses continue to be financed by appropriations from the state medical society, registration fees and the state department of health. The total income, including registration fees and appropriation from the state society, is approximately $1,500, which, together with the support from the state department of health and the organization and administration service donated by the extension division of the University of Virginia, has been sufficient to continue the program.

INSTRUCTION FOR NEGRO PHYSICIANS

The first postgraduate clinic for Negro physicians was held at the St. Philip Clinic, Medical College of Virginia, in June 1931. It was felt that there was need for better trained Negro physicians, and it was recognized that adequate postgraduate clinic facilities should be provided to keep them abreast of advances in medicine. The St. Philip Hospital for Negroes accommodates 131 patients in teaching wards and has laboratories available for special study. The General Education Board of New York City has given financial aid from the beginning. The Negro state and local medical associations cooperated in sponsoring this educational venture. Each year two weeks courses are offered to a group of from eighteen to forty-two colored physicians. A registration fee of $10 is charged. Six hours is devoted each day to classes. There

are lectures, assignments of patients in the wards, demonstrations and bedside teaching. Instruction includes chiefly medicine as well as surgery, obstetrics and gynecology, clinical pathology, pediatrics and public health. Round table discussions are held on alternate days. Members of the first class met with members of the faculty and developed a plan providing for individual instruction. Each year one or more out of state physicians aid the medical college faculty in the instruction. In the fourth year clinical pathologic conferences featured the instruction and in the fifth year there were ten two hour periods devoted to surgical anatomy with actual dissection by members of the class. In that year seventy-nine members of the college faculty participated in the instruction.

Of those who registered for the St. Philip Hospital postgraduate clinics, approximately half practice outside of Richmond. Other than Virginia physicians, most of the applicants come from North Carolina, although such states as Alabama, Florida, Kentucky, Missouri, South Carolina, Tennessee and Texas have been represented.

Negro physicians who have attended these clinics petitioned the governor of the state to provide financial aid for their continuance. The state legislature however failed to provide sufficient funds, but the instruction continues each year at a cost of approximately $1,250. This includes honorariums and expenses for publicizing the enterprise. Richmond physicians who have enrolled for this instruction in the past have requested the faculty of the Medical College of Virginia to aid them in giving additional postgraduate instruction during the year between the postgraduate clinics.

OTHER POSTGRADUATE ACTIVITIES

The Richmond Academy of Medicine gave a symposium on hematology, consisting of seven lectures which began in October 1938 and ended in February 1939. Six instructors from the medical schools of Virginia and an out of state medical school instructor comprised the faculty. Sixty-six practicing physicians attended this lecture series. A registration fee of $3 was charged.

The library of the Medical College of Virginia offers a package medical service to any physician in the state who will pay the return postage on packages. From 120 to 150 out of town physicians use this service each year.

Of the 2,818 physicians licensed in the state of Virginia, 1,761 are members of the state medical society.

CORRECTION

DISTRICT OF COLUMBIA

In THE JOURNAL, July 15, page 237, there were said to be 2,141 physicians licensed to practice in the District of Columbia, of whom 872 are members of the Medical Society of the District of Columbia. The executive secretary of the society has since reported that there are 1,901 physicians licensed to practice in the District of Columbia, of which number it is estimated that from 1,000 to 1,100 are engaged in private practice, the remainder being employed by the district or federal government or have retired. The Medical Society of the District of Columbia at present has 885 active members, 169 associate members and seven honorary members, a total of 1,061.

MEDICAL LEGISLATION

DISTRICT OF COLUMBIA

Changes in Status.—The following bills have passed the Senate: S. 2745, authorizing the Commissioners of the District to promulgate and enforce all such reasonable rules and regulations as they may deem necessary to prevent and control the spread of communicable diseases in the District of Columbia; S. 2779, proposing to eliminate from the healing arts practice act in the District of Columbia the requirement that examinations be held on the second Monday in January and July of each year and to provide that such examinations may be held at such times as the Commission on Licensure to Practice the Healing Art may by rule or by special order determine; H. R. 4732 and H. R. 4733, proposing, respectively, to provide for the issuance of a license to practice chiropractic in the District of Columbia to George M. Corriveau and to Laura T. Corriveau; H. R. 6266, providing for the incorporation of certain persons as Group Hospitalization, Inc., the corporation to be authorized to enter into contracts with individuals or groups of individuals to provide for hospitalization of such individuals, to enter into contracts with hospitals for the care and treatment of such individuals, and to cooperate, consolidate or contract with groups or organizations interested in promoting and safeguarding the public health; and H. R. 7086, proposing to provide for insanity proceedings in the District of Columbia.

MEDICAL BILLS IN CONGRESS

Changes in Status.—S. 1540 has passed the House with amendments, proposing to increase the compensation of members of the National Advisory Health Council not in the regular employment of the government. A preliminary report on S. 1620 has been submitted to the Senate by the Senate Committee on Education and Labor. S. 1620 proposes to provide for the general welfare by enabling the several states to make more adequate provision for public health, prevention and control of disease, maternal and child health services, construction and maintenance of medical hospitals and health centers, care of the sick, disability insurance, and training of personnel. The Committee announced that a subcommittee appointed by it to consider the bill reported that it is in agreement with the general purposes and objectives of the bill but wishes to give additional study to it and to consult further with representatives of lay organizations and of the professions concerned, in contemplation of reporting out an amended bill at the next session of Congress. S. 1899 has passed the House, providing for the detail of a commissioned medical officer of the Public Health Service to serve as assistant to the Surgeon General. S. 2284 has passed the Senate, authorizing the President to appoint 100 acting assistant surgeons for temporary service in the Navy. Senator Walsh, Massachusetts, explained that, whereas in the past mistakes had been made from time to time in giving permanent appointments to appointees who had not been tried out in the naval service, the purpose of the bill is to do away with permanent appointments until after appointees for temporary service have served a probationary period of eighteen months to determine their fitness and capability to perform the medical work required of surgeons in the Navy. It is contemplated that twenty-five of the 100 appointed will be eliminated so that the usual number of seventy-five permanent appointments will be made, as that number of surgeons yearly are required to take care of the health of the officers and enlisted men of the Navy. H. R. 6555 has passed the Senate, proposing to amend the law relating to the advance of funds in connection with the enforcement of acts relating to narcotic drugs, so as to permit such advances in connection with the enforcement of the Marihuana Tax Act of 1937. H. R. 6635, proposing to amend the Social Security Act, has been passed. As passed, the bill authorizes an increase in appropriations for maternal and child health services and services for chippled children, under the supervision and control of the Children's Bureau, and in appropriations for public health activities, under the supervision and control of the Public Health Service. An amendment, adopted by the Senate on the motion of Senator Wagner, to create an advisory council on disability insurance, to be established by the Committee on Finance of the Senate and the Committee on Ways and Means of the House of Representatives, in cooperation with the Social Security Board, was eliminated in conference.

Bill Introduced.—S. 2963, introduced by Senator Lodge, Massachusetts, proposes to amend the Social Security Act by adding a title XII, providing for a system of health insurance to

assist "qualified individuals to receive medical services when they require such care but are without means." A "qualified individual" is defined as one who has been registered as unemployed for at least fifteen consecutive weeks at a public employment office or other agency approved by the Social Security Board; is not receiving old-age benefits; before attaining the age of 65 has been paid, after Dec. 31, 1936, not less than $5,000 in total wages from an employment as defined in section 210(b) of the Social Security Act; and has filed (1) an application for health insurance benefits, (2) a bill for medical or hospital services rendered to him and (3) the sworn affidavit of the attending medical practitioner or of the medical supervisor of the hospital that such medical or hospital treatment was furnished. It is proposed that every qualified individual shall be entitled in any year, on approval of his application by the Social Security Board, "to have forwarded to the doctor or hospital furnishing him with medical or hospital services, in part or full payment, for such services a sum equal to all or to any part of the health-insurance benefit to which such individual is entitled for such year," such benefit to be equal to one fifth of 1 per cent of such individual's total wages, except that such benefit shall not be in excess of $25 for one year and the total of all such benefits shall not be in excess of $100. The bill further proposes that any doctor participating in any false statement in connection with an application for benefits shall be reported by the Social Security Board to the state medical authority which issues and revokes licenses to practice medicine.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARIZONA

Personal.—Dr. Louis J. Saxe has been appointed superintendent of the Arizona State Hospital at Phoenix.——Dr. Frederick P. Perkins, Florence, who was for eleven years director of health at the University of Arizona, Tucson, has been appointed tuberculosis consultant to the state board of health.

Harlow Brooks Memorial Conference.—The fourth Harlow Brooks Memorial Navajo Clinical Conference will be held at the Sage Memorial Hospital, Ganado, August 28-30. The speakers will include:

Dr. George W. Crile, Cleveland, The Antithetic Influence of Reason and Emotion in the Genesis of Coronary Disease and Hypertension.
Dr. Ray M. Balyeat, Oklahoma City, Diagnosis and Treatment of Common Allergic Manifestations Encountered by the General Practitioner; Diagnostic and Therapeutic Value of the Use of Iodized Oil in Chronic Asthma and Bronchiectasis.
Dr. Max Thorek, Chicago, Advantages of Electrosurgical Obliteration of the Gallbladder Over Classical Cholecystectomy.
Dr. Thomas G. Orr, Kansas City, Mo., Treatment of Fresh Wounds and Wound Healing; Management of Acute Intestinal Obstruction.
Dr. Phil W. Shumaker, Los Angeles, Intragastric Photography.
Dr. William H. Daniel, Los Angeles, Cancer of the Rectum.
Dr. Frank R. Teachenor, Kansas City, Mo., Surgical Relief of Intractable Pain.
Dr. William Warner Watkins, Phoenix, Correlation of Clinical and Roentgenological Evidence in Chest Disease.
Dr. Charles A. Thomas, Tucson, Extrapleural Pneumothorax in Tuberculosis.

The registration fee for the conference is $3, which covers all expenses. Rooms or dormitory space will be provided and meals will be served in the school dining room.

CALIFORNIA

Plague Infection.—According to *Public Health Reports*, June 23, plague infection has been proved in six ground squirrels, Citellus beecheyi, submitted to the laboratory of the state department of health April 25, from a point 1½ miles north of Rincon, Ventura County.

Courses for Practitioners.—Stanford University School of Medicine, cooperating with the San Francisco department of public health and the San Francisco Hospital, will offer a series of postgraduate medical courses for practicing physicians August 28-September 1. Morning courses will cover traumatic injuries and fractures, obstetrics, diseases of the genito-urinary tract and cardiology, while the afternoon courses will be given over to diagnosis and treatment of malignant tumors, allergic diseases, neurology and psychiatry and surgical anatomy and operative technic. Ophthalmology and anesthesiology will be considered in the courses for specialists. The speakers at general meetings will be:

Dr. Frederick L. Reichert, August 29, Peripheral Vascular Diseases.
Dr. Garnett Cheney, August 30, Vitamin Therapy.
Drs. Harry E. Alderson, San Francisco, and Merlin T.-R. Maynard, San Jose, August 31, Problems in Dermatology.

CONNECTICUT

New Society of Physical Therapy.—The Connecticut State Physical Therapy Society was recently organized with Drs. Harry E. Stewart, New Haven, president; Robert E. Peck, New Haven, and Charles Edlin, Waterbury, vice presidents, and Karl B. Bretzfelder, New Haven, secretary. The society was formally made a section of the Connecticut State Medical Society at its recent annual session.

DELAWARE

Society News.—Dr. Frederic H. Leavitt, assistant professor of neurology, Jefferson Medical College of Philadelphia, addressed the New Castle County Medical Society recently on "Trauma and the Central Nervous System."

Changes in State Board.—Dr. Arthur C. Jost, Dover, has resigned as executive secretary of the state board of health, effective August 10, according to the Wilmington *News*. Dr. Robert E. Ellegood, who has been a member of the board for twenty-three years, has also resigned, it was stated. Dr. Jost became executive secretary of the board Jan. 1, 1929, succeeding Dr. Arthur T. Davis, now at Riverhead, N. Y. He had formerly served as a county health officer in Nova Scotia and for ten years was in the provincial health department.

DISTRICT OF COLUMBIA

Mutual Health Service Begins.—The Mutual Health Service of the Medical Society of the District of Columbia was placed in operation July 1. Through this agency people of low incomes will be enabled to spread the cost of illness over a long period of time, according to *Medical Annals*.

Cornerstone Laid for Doctors' Hospital.—Ceremonies for laying the cornerstone of the new Doctors' Hospital were held in Washington July 11. Dr. Charles Stanley White is president of Doctors' Hospital, Inc. The principal speaker was Senator Robert A. Taft of Ohio. Among the guests were Drs. George C. Ruhland, District health officer; Lewis H. Taylor, president, Sibley Hospital; Thomas Parran, surgeon general, U. S. Public Health Service; William C. Woodward, former health officer of the District and now Director of the Bureau of Legal Medicine and Legislation, American Medical Association, Chicago, and Francis J. Eisenman, superintendent, Garfield Memorial Hospital. The $1,500,000 Doctors' Hospital will be ten stories high and will offer accommodations for 250 patients. It will connect the two medical buildings, known as the Washington and Columbia Medical Buildings, which have as tenants about 250 physicians and representatives of the allied professions. Mr. Charles E. Vadakin, former manager of the Kahler Hospital, Rochester, Minn., will be superintendent.

FLORIDA

Personal.—Dr. Grady H. W. Brantley is the new mayor of Lake Worth, it is reported.——Dr. Leland J. Hanchett, passed assistant surgeon, U. S. Public Health Service, has been placed in charge of the division of venereal disease control of the state board of health, relieving Dr. Leo C. Gonzalez, Jacksonville, while he is taking a postgraduate course in venereal disease control and public health at Johns Hopkins University School of Hygiene and Public Health, Baltimore.

County Society Sponsors Newspaper Supplement.—A forty page medical section in tabloid form, sponsored by the Escambia County Medical Society, was published by the Pensacola *News-Journal* on Sunday, July 23. Among the features of the section were articles on the federal government and the medical profession, prepared by the executive committee of the Nassau County (N. Y.) Medical Society; an outline of the way in which the American Medical Association serves the profession and the American people, and numerous illustrated articles on various phases of medicine and public health. No by-lines of any members of the society were used. In a special announcement it was stated that the section was published under the sponsorship of the society; a committee passed on the news matter and advertisements. A list of the names of the society's officers and members followed.

113
939

ILLINOIS

Society News.—At a joint meeting of the Fulton and McDonough county medical societies in Bushnell June 20 Drs. James C. Redington and Frederic E. Hambrecht, Galesburg, spoke on "The Diagnosis of Pulmonary Tuberculosis" and "Surgical Treatment of Pulmonary Tuberculosis" respectively. ——Dr. James J. Callahan, Chicago, discussed fractures before the Effingham County Medical Society in Effingham June 13.

Chicago

Resurvey of Venereal Diseases.—To determine the effectiveness of efforts toward the control of venereal diseases, a resurvey of all treatment sources is being planned in accordance with a request from Dr. Thomas Parran, surgeon general, U. S. Public Health Service, according to the Chicago Medical Society *Bulletin*. A campaign was begun throughout the state in June 1937 to bring patients with syphilis under medical care.

Retires as Professor of Oral Surgery.—Dr. Herbert A. Potts, for many years professor of oral surgery at Northwestern University medical and dental schools, will retire from the dental school at the end of the academic year September 1, with the title of professor emeritus. Dr. Potts, who also has the degree of doctor of dental surgery, has been associated with Northwestern University Dental School since 1908, first as lecturer in anesthesia, assistant in oral surgery, professor of pathology, instructor in oral surgery, assistant professor and since 1921 professor of oral surgery. He received his degree in dentistry at Northwestern in 1895 and his medical degree in 1901. He retired from the medical school as professor emeritus June 30, 1938.

Lay Cornerstone of Neuropsychiatric Institute.—The cornerstone of the Neuropsychiatric Institute, University of Illinois College of Medicine, was laid with appropriate ceremonies recently. Addresses were delivered, among others, by Arthur Cutts Willard, LL.D., president, University of Illinois; D. R. Kennicott, regional director, PWA; Dr. Richard H. Hutchings, Utica, N. Y., and Dr. Adolf Meyer, Baltimore. The cornerstone was laid by A. L. Bowen, director of the state department of public welfare, and the invocation given by Rev. Arthur E. Johnstone of the Episcopal City Missions. The building is expected to be ready for occupancy in the fall of 1940. More than $500,000 of the approximate cost of $1,300,000 has been supplied by PWA funds. The building, which will be eleven stories high, will be used for teaching neurology and psychiatry and for research in these fields (THE JOURNAL, Aug. 27, 1938, p. 851).

Annual Report of Tumor Institute.—A total of 505 patients representing twenty-two states, Canada, Cuba, South America and Spain were treated at the Chicago Tumor Institute during its first year of operation, according to its initial report recently released. Seventeen indigent patients were cared for without any referring physicians. There were 4,772 examinations made during the year; 1,299 x-ray diagnostic procedures and 1,975 treatments given with radium and 3,576 with x-ray. There were about twenty-five classifications of the types of cancer. Leading the list were: cancer of the breast, 104 cases; larynx, forty-three; cervix and uterus, twenty-six each, and tongue, twenty-three. The report acknowledges the arrangement with the veterans' hospital at Hines which has enabled the institute to utilize the clinical material at Hines to project special research on cancer of the larynx. The report emphasizes the need of an experimental laboratory to supplement the clinical investigations. Space is available but funds do not permit this activity. Another need of the institute is a library of current periodicals and monographs on cancer. Duing the year postgraduate instruction was given to about fifty specialists from all parts of the United States and from Hawaii, Cuba and South America. The teaching program of the institute is being developed on a comprehensive scale. The report classifies the program as follows: one year fellowships or traineeships; visiting fellows (from one to six months); postgraduate instruction to radiologists (from one to three months); short annual courses (one week) and weekly cancer clinics for fourth year students at Northwestern University Medical School (ninety students). The Chicago Tumor Institute, opened in March 1938, was chartered in Illinois, not for profit, to conduct research on the causes, diagnosis and treatment of cancer and to train cancer specialists. The institute has available 11 Gm. of radium, 10 Gm. of which is used in the form of a radium bomb. Dr. Max Cutler is director of the institute and Dr. Ludvig Hektoen is president of the board of trustees.

INDIANA

Personal.—Dr. Wesley M. Hoppenrath, Elwood, has been appointed regional medical examiner for the Civil Aeronautics Authority.——Dr. and Mrs. Joseph L. Reeve, Edwardsport, celebrated their golden wedding anniversary recently.

Hospital News.—A cancer institute will be established at the Protestant Deaconess Hospital, Evansville, next fall, it is reported. Dr. Keith T. Meyer, Evansville, will be in charge of the institute, which is said to be one of a series set up throughout the country under the auspices of the American College of Surgeons. Equipment valued at $15,000 will be installed at the beginning and more will be added later.

IOWA

Personal.—The Dubuque County Medical Society held a special meeting in Sageville June 20 to observe the completion of fifty years in the practice of medicine by Dr. Bernard A. Michel, Dubuque. Drs. Martin E. Dittmer, Colesburg, who has practiced in Colesburg for fifty-two years, and John C. Dennison, who has practiced in Bellevue, for fifty years, were also guests of honor.

Society News.—Dr. Philip C. Jeans, Iowa City, discussed pediatrics before a joint meeting of the Bremer County Medical Society and the staff of Mercy Hospital at the Fortner Hotel, Waverly, June 28.——At a meeting of the Greene County Medical Society in Jefferson June 8 Dr. William F. Mengert, Iowa City, spoke on "The Management of Complicated Labor." ——Dr. Lewis M. Overton, Des Moines, discussed common fractures before the Henry County Medical Society June 6.—— Dr. Conan J. Peisen, Des Moines, addressed the Jasper County Medical Society in Newton June 13 on peptic ulcers.

LOUISIANA

Changes in Health Directors.—Dr. Lailor A. Morrogh, Jr., Arnaudville, has been appointed director of the Avoyelles Parish health unit, succeeding the late Dr. Lucius W. Holloman, Marksville.——Dr. Bert L. Stinson, Homer, has succeeded Dr. Walter W. Poimboeuf as head of the health service in Claiborne Parish.——Dr. Christopher L. Mengis, New Orleans, formerly director of the crippled children's division of the state board of health, has been appointed to succeed Dr. Stinson as director of the Iberia Parish health unit.

Dr. Barber Made President of State Society.—Dr. Dorman B. Barber, Alexandria, has been made president of the Louisiana State Medical Society. He succeeds Dr. Clarence A. Lorio, Baton Rouge, who resigned following his indictment for embezzlement of Louisiana State University property. Dr. Barber graduated at Tulane University of Louisiana School of Medicine, New Orleans, in 1926. He is 39 years of age. Dr. Barber was first vice president of the medical society. Dr. Edwin L. J. Zander, New Orleans, was advanced from second to first vice president; Dr. Jean P. Mauboules Jr., Rayne, from third to second, and Dr. Walter O. Moss, Lake Charles, was appointed third vice president.

MICHIGAN

Society News.—Dr. Fred Z. Havens, Rochester, Minn., discussed plastic surgery before the Muskegon County Medical Society June 16.—— Dr. Willard O. Thompson, Chicago, addressed the Berrien County Medical Society, Benton Harbor, July 13, on "Clinical Application of Male Sex Hormone in the Treatment of Disease."

Program of Postgraduate Education Expands.—The advisory council on postgraduate medicine of the Wayne County Medical Society, Detroit, has elected officers, including a registrar, secretary and executive secretary and formally launched "The Continuation School of Medicine of Wayne County," according to Detroit *Medical News*. The "school" proposes to offer courses in the specialties to general practitioners, using the facilities of the Wayne County Medical Society, the Detroit department of health, the hospitals, the department of welfare and the Wayne University College of Medicine. The courses will begin in the fall and will start with bedside teaching of general medicine for physicians in groups of from four to six. The days and hours chosen will be determined by mutual arrangement of the hospitals, the practitioners and the teachers. Gradually, as the advisory council directs, other courses will be added on a basis of the highest teaching standards. It is probable that the next one will be on pathology.

Dr. William J. Stapleton Jr. is registrar of the "school"; Dr. David I. Sugar, secretary, and James A. Bechtel, LL.B., executive secretary. Executive management of the project will be governed by these officers, the executive officers of the county medical society and an advisory council.

Poliomyelitis Appears in Michigan.—Fifty-four active cases of poliomyelitis were reported from Detroit and eighteen from other parts of the state August 6. Since January 1 there have been ninety-two cases in the city, most of them since July 1. There have been six deaths in the recent cases. Scattered cases have been reported outside of Detroit, as follows: Saginaw, three cases; Oakland County, seven; Monroe, six; Calhoun, one, and Muskegon, one. Plans for combating the outbreak have been announced by local and state medical societies and health authorities. The committee on preventive medicine of the Michigan State Medical Society held a meeting in Detroit August 2 under the chairmanship of Dr. Ledru O. Geib, Detroit, at which arrangements were made for consultation service. Members of the American Academy of Pediatrics and the Michigan Orthopedic Society have agreed to render this service, which may be arranged through the office of the state medical society in Lansing. The state society has distributed about 2,000 copies of a brochure on poliomyelitis published by the American Medical Association to officers of county medical societies and physicians in the affected areas. The Detroit Department of Health has distributed literature to Detroit physicians and the Wayne County Medical Society has also been active. A conference was held July 31 with Dr. Edgar E. Martmer, chairman of the county society's committee on preventive medicine, as leader of the discussion. The National Foundation for Infantile Paralysis has allocated $12,000 to finance an experimental laboratory to be established at Lansing under the direction of Dr. Sidney D. Kramer, Brooklyn, it was announced July 28. The Foundation will also provide funds for a respirator at Herman Kiefer Hospital, Detroit. Drs. James D. Trask, associate professor of pediatrics, and John R. Paul, associate professor of medicine, Yale University School of Medicine, New Haven, have been invited to lecture on poliomyelitis at a postgraduate conference at the hospital August 16. Dr. Alexander G. Gilliam of the U. S. Public Health Service is also in the state in connection with the outbreak. The public health service is reported to have made a grant of $5,000 to aid in the establishment of the laboratory at Lansing. In addition to the Michigan outbreak, Sarnia, Ont., directly across the border from Port Huron, has reported nineteen cases with five deaths. The Ontario government has established a special laboratory in Sarnia to aid in handling the work.

MINNESOTA

Physicians Honored.—At a meeting of the council during the annual session of the Minnesota State Medical Association May 31-June 2 it was voted to present the distinguished service medal and scroll, awarded to members for special contribution to the work of the association, to the late Drs. William J. Mayo and Charles H. Mayo, Rochester, and Herman M. Johnson, Dawson. According to the state medical journal, photographs of the three will be hung at the University of Minnesota Medical School, Minneapolis. Dr. William Mayo died July 28.

MISSOURI

Personal.—Dr. John Aull, Kansas City, has been appointed a member of the state board of health.——Dr. Frank R. Bradley, St. Louis, has been appointed superintendent of Barnes Hospital, St. Louis, succeeding Dr. Louis H. Burlingham, who recently resigned, it is reported. Dr. Oswald N. Andersen, Chicago, a member of the staff of the Council on Medical Education and Hospitals, American Medical Association, has been appointed assistant superintendent.——Philip Anderson Shaffer, Ph.D., dean, Washington University School of Medicine, St. Louis, was awarded the honorary degree of doctor of science by the University of Rochester, Rochester, N. Y., at its recent annual commencement.

MONTANA

State Medical Election.—Dr. James I. Wernham, Billings, was chosen president-elect of the Medical Association of Montana at its annual session in Butte July 1 and Dr. Harold W. Gregg, Butte, was installed as president. Dr. Thomas F. Walker, Great Falls, was elected secretary, succeeding Dr. Thomas L. Hawkins, Helena, who had held the office since 1937.

NEW JERSEY

Law Authorizes Blood Tests for Paternity.—Authority to order blood tests in cases of disputed paternity is granted in a law passed by the state legislature and signed by Governor Moore July 18. The law requires that the tests be made by duly qualified physicians to be appointed by the court. This is the fourth law of its kind to be enacted by a state, the other states being Ohio, New York and Wisconsin.

NEW YORK

Annual Chautauqua Meeting.—The eighth annual interstate meeting of the Medical Society of the County of Chautauqua was held at Chautauqua Institution July 26. In the morning there was a scientific session with the following speakers: Drs. Arthur C. Christie, Washington, D. C., on "Diagnosis and Management of Cancer of the Breast"; George E. Hall, Toronto, Ont., "Reduction of Mortality Following Coronary Occlusion," and Russell L. Cecil, New York, "Sulfapyridine in the Treatment of Pneumonia." In the afternoon Dr. Christie and Dr. Cecil gave addresses at a public meeting.

Executive Secretary Dies.—Mr. Samuel A. Matthieu, executive secretary of the Medical Society of the County of Erie, Buffalo, died July 22 at his home, aged 67. Mr. Matthieu had been with the medical society for thirteen years. He was at one time associated with the New York *Times*.

New York City

Personal.—An item in THE JOURNAL July 22, page 342, announced that Dr. Philip R. Lehrman was recently promoted to be clinical professor of neurology and psychiatry at Columbia University College of Physicians and Surgeons. Dr. Lehrman writes that this should have been the New York Postgraduate Medical School and Hospital.——Dr. Israel S. Wechsler will present a paper at the Third International Neurological Congress in Copenhagen, August 21-25, on "Avitaminosis and Peripheral Neuropathies."

City Hospital Receives First Patients.—The city's new $8,000,000 Hospital for Chronic Diseases on Welfare Island received its first patients July 6. Two hundred were transferred from City Hospital, also on the island. Within the next week 400 were to be moved from the old Neurological Hospital, 100 from Metropolitan Hospital, both on the island. In addition, 400 were to be brought from Kings County Hospital, Brooklyn. Twenty-four wards were to be occupied, leaving eight to be filled later. Dr. Chrisman G. Scherf is superintendent of the new hospital.

Physician Wins Refund on Telephone Rate.—A municipal court justice handed down a decision July 6 that a physician who maintains his office in his home is entitled to pay residence telephone rates, the New York *Times* reported July 7. The decision ordered the New York Telephone Company to pay Dr. Henry C. Eichacker $131.56, representing the difference between the office rate and the residence rate from Jan. 7, 1931 to Oct. 1, 1936. The physician originally asked a refund from 1923, but the additional time was ruled out under the statute of limitations. The case had been previously heard by a different justice, who dismissed it. A new trial was granted after an appeal. It was said that if the ruling were upheld on appeal to a higher court, the telephone company would have to refund more than $2,000,000 to physician subscribers in its territory.

NORTH CAROLINA

Changes in Health Officers.—Dr. Joseph A. Morris, Oxford, has retired as health officer of Granville County after twenty years of service. His successor is Dr. Ballard Norwood Jr., Oxford.——Dr. Wesley G. Byerly, Statesville, has been appointed health officer of the Burke-Caldwell district health department, succeeding Dr. Warren D. Carter, Morganton. ——Dr. Clarence H. White, Newton, has resigned as health officer of Catawba County to study at Harvard University.

Society News.—Drs. Lowell H. Coleman, Spartanburg, S. C., and Lewis W. Hagna, Marion, among others, addressed the Thermal Belt Medical Society in Saluda July 20 on "Common Disorders of the Feet" and "Prognosis in Rheumatic Fever" respectively.——Dr. Claude G. Mentzer, Miami, Fla., was the guest speaker at a meeting of the Catawba Valley Medical Society, Lincolnton, July 14, on "Pathogenesis of Diseases of the Anal Region."——Dr. George M. Cooper of the state board of health, Raleigh, addressed the Johnston County Medical Society at Princeton June 27 on the board's work on infant and maternal care.——Drs. Charles J. Bloom, New Orleans, and Warren W. Quillian, Coral Gables, Fla., addressed the Buncombe County Medical Society, Asheville, July 31, on "Spastic Colitis in Infants and Children" and "Convulsions in Infants and Children" respectively.

NORTH DAKOTA

Society News.—Dr. John H. Moore, Grand Forks, was elected president of the North Dakota Society of Obstetrics and Gynecology at a meeting in Fargo recently; Dr. Albert M. Brandt, Bismarck, vice president, and Dr. August C. Orr, Bismarck, secretary.

OHIO

Professor Retires.—Dr. Elmer G. Horton, clinical professor and chairman of the department of pediatrics, Ohio State University College of Medicine, Columbus, has retired after thirty-seven years as a member of the faculty. Dr. Horton graduated in medicine at Ohio State in 1906 after having been professor of hygiene and physical culture at Wabash College, 1893-1895; instructor in hygiene, University of Pennsylvania, 1896-1898. He was also bacteriologist and chemist for the state board of health laboratories, 1898-1907, and health commissioner of Columbus, 1907-1909. He became assistant professor of pediatrics at Ohio State in 1914 and professor in 1924. He has been clinical professor since 1937.

PENNSYLVANIA

District Meetings.—The annual meeting of the Fourth Councilor District of the Medical Society of the State of Pennsylvania was held at Ashland June 29. The speakers were Drs. Edward L. Bortz, Philadelphia, chairman of the state society's commission on pneumonia control, on "Modern Treatment of Pneumonia, Including a Discussion of Sulfapyridine"; Belford C. Blaine, Pottsville, chairman of the commission on diabetes, "Diabetes—the Family Physician's Problem"; David W. Thomas, Lock Haven, president of the state society, "Medicine Faces Crisis," and Walter F. Donaldson, secretary, Pittsburgh, "The National Scene." The same speakers addressed a meeting of the Twelfth Councilor District at Dallas June 28 and in addition Dr. Rufus S. Reeves, Philadelphia, spoke on "The Role of the Clinician in the Health Department's Division of Cancer Control." Mrs. John H. Doane, Mansfield, president-elect of the Woman's Auxiliary to the state society, and Mrs. Donaldson, the present president, addressed meetings of the auxiliaries on both occasions.

Philadelphia

Blakiston Firm Changes Hands.—The publishing house of P. Blakiston's Son & Co., Inc., specializing in scientific and medical books, has been purchased from the estate of Kenneth M. Blakiston by Mr. Horace G. White, who has been executive vice president of the firm. The business was established in 1843 by Presley Blakiston and was continuously in the Blakiston family until the death of Kenneth M. Blakiston in 1937. It will now be carried on under the name The Blakiston Company. Mr. White will be president; Charles C. Norris Jr., and Robert F. Bowman, vice presidents; Edmund J. Glaser, treasurer, and Edward B. Barnes, secretary.

SOUTH CAROLINA

Dr. Guerry Honored.—Friends of Dr. LeGrand Guerry, Columbia, recently presented a bust of him to Columbia Hospital, where he has been surgeon since 1900. At the unveiling ceremony June 1 Reed Smith, Ph.D., professor of English at the University of South Carolina, made the principal address and two grandsons of Dr. Guerry unveiled the bust. Dr. Guerry graduated from the University of Georgia School of Medicine, Augusta, in 1896. He has been president of the South Carolina Medical Association, the Southern Surgical Association and the Tri-State Medical Association.

TENNESSEE

Society News.—Dr. Fred H. Albee, New York, addressed the Sullivan-Johnson Counties Medical Society at a meeting in Bristol, Va., June 7, on "The Surgical Use of Bacteriophage."——Drs. Robert Lyle Motley and William Milton Adams, Memphis, among others, addressed the Dyer, Lake and Crockett Counties Medical Society at a meeting at Reelfoot Lake June 7 on "Medical Treatment of Gallbladder Disease" and "Modern Concepts in the Treatment of Compound Facial Injuries" respectively.——At a meeting of the Five-County Medical Society (Hardin, Lawrence, Lewis, Perry and Wayne Counties) in Waynesboro June 27 the speakers were Drs. Charles Fowler Hollabaugh, Nashville, on "Management of the More Common External Diseases of the Eye"; Alva A. Jackson, Florence, Ala., "Conservative Treatment of Gallbladder Disease," and Murray B. Davis, Nashville, "Injuries of the Chest."——Dr. John S. Hawkins, Springfield, addressed the Robertson County Medical Society June 20 on toxemias of pregnancy.

VIRGINIA

Changes in Health Officers.—Dr. John C. Neale Jr., Staunton, has resigned as health officer of Augusta County and Dr. Vernon A. Turner, Richlands, formerly in charge of the Buchanan-Russell-Tazewell district, will succeed him. Dr. Neale will be in charge of the southwest district with headquarters at Abingdon. Dr. George R. Carpenter, formerly of Bristol, has been appointed health officer of Fairfax County to succeed Dr. Edward M. Holmes Jr., now on the staff of the state health department. Other appointments are: Dr. John B. H. Bonner, transferred from Prince George County to the Page-Shenandoah-Warren health district, Luray; Dr. Francis J. Clements, Stony Creek, from Sussex County to the Sussex-Prince George health district, Stony Creek; Dr. Chester L. Riley, Manassas, from Prince William County to the Prince William-Stafford health district, Manassas. Dr. Paul W. Bowden, Franklin, has been appointed health officer of Southampton County, succeeding the late Dr. Peter P. Causey, Courtland.

WEST VIRGINIA

Conferences on Obstetrics and Pediatrics.—A series of postgraduate conferences in obstetrics and pediatrics is in progress in ten towns forming two circuits under the auspices of the division of maternal and child hygiene of the West Virginia State Health Department and the maternal and child welfare committees of the West Virginia State Medical Association. In the southern section Dr. William J. Dieckmann, Chicago, is giving three lectures in obstetrics at weekly intervals and Dr. Edward L. Bauer, Philadelphia, two lectures in pediatrics. The towns in the southern circuit are: Bluefield, Williamson, Huntington, Beckley and Ronceverte. In the northern circuit Drs. Everett D. Plass and William F. Mengert, Iowa City, are lecturing on obstetrics and Dr. Lee Palmer, Louisville, Ky., on pediatrics in Weirton, Moundsville, Buckhannon, Elkins and Keyser. The series began July 17 and will end August 18.

WISCONSIN

Society News.—At a meeting of the Wood County Medical Society in Wisconsin Rapids, June 15, the speakers were Drs. Robert W. Mason, Marshfield, and Rogers E. Garrison, Wisconsin Rapids, on "Dislocation of Cervical Vertebrae"; Karl H. Doege, Marshfield, "Buerger's Disease with Myocardial Insufficiency"; Robert S. Baldwin, Marshfield, "Diabetic Gangrene," and Leo M. Morse, Neillsville, "Equine Encephalomyelitis."——Dr. Harold E. Marsh, Madison, addressed the Trempealeau-Jackson-Buffalo Tri-County Medical Society, Black River Falls, June 15, on "Cardiac Irregularities, Methods of Diagnosis and Treatment."

GENERAL

Society Urges Care for Handicapped Children.—The American Laryngological Association at its recent annual meeting adopted a resolution urging adequate programs for detection and correction of visual, hearing and speech handicaps in school children. The resolution points out that in many communities and rural districts little or no attention has been paid by school authorities to these disabilities affecting children. It then recommended "the provision of funds by foundations and other appropriate agencies to carry out adequate programs for the detection of visual, hearing and speech deficiencies which constitute a handicap to school children, and, for providing through the cooperation of qualified specialists and of state, county and local medical societies appropriate medical care for indigent and underprivileged children who may be afflicted or threatened with such handicaps."

Change in Date of Examination and Fees for Obstetric Board.—The next written examination and review of case histories (part I) for group B candidates of the American Board of Obstetrics and Gynecology will be held in various cities of the United States and Canada January 6, 1940, instead of December 2 as the board heretofore announced. Increases in the fees for the application and examination have been announced as $15 and $85 respectively. The Board announces that it will hold only one group B, part I, examination this year prior to the final general examination, instead of two as in former years. Candidates who successfully complete the part I examination proceed automatically to the part II examination held in June 1940. Application for admission to group B, part I, examinations must be on file in the secretary's office not later than October 4. Dr. Paul Titus, 1015 Highland Building, Pittsburgh, is the secretary.

Society News.—The twenty-fourth National Recreation Congress will be held in Boston October 9-13. Additional information may be obtained from Mr. T. E. Rivers, secretary, National Recreation Association, 315 Fourth Avenue, New York City.——The Tri-State Medical Society (Arkansas, Louisiana and Texas) will hold its annual meeting at Marshall, Texas, November 8-9. Additional information may be obtained from Dr. Paul D. Abramson, chairman, program committee, 1130 Louisiana Avenue, Shreveport, La. Dr. Joseph D. Roberts Jr., Longview, Texas, is president.——The fifth International Congress for the Unity of Science will be held at Harvard University, Cambridge, Mass., September 3-9. Secretaries of the congress are Prof. Otto Neurath, International Institute for the Unity of Science, 267 Obrechtstraat, The Hague, Holland, and Charles W. Morris, professor of philosophy, University of Chicago.

Congress on Military Medicine.—Thirty-five governments were represented at the recent Tenth International Congress of Military Medicine and Pharmacy, held in Washington, D. C., May 7-15. The congress was followed by the ninth session of the International Office of Documentation of Military Medicine in New York May 15-19. Secretary of State Cordell Hull addressed the delegates in Washington. In addition to the scientific program, they visited Walter Reed Hospital, the Army Medical Museum, the Army Medical Library, the U. S. Naval Academy at Annapolis, the U. S. Military Academy at West Point and the medical field service school at Carlisle Barracks, Pa. Topics on the program included: organization and function of sanitary service in colonial expeditions; methods of determining the number of casualties; practical procedures for anesthesia and analgesia in war surgery; organization and functioning of the military chemicopharmaceutical service; treatment of fractures of the maxillary bones; oxygen therapy and technical specialization for administrative officers in the medical services. It was proposed that an "institute of graduate medicomilitary studies" be created and opinions of each country are to be sent to the secretary-general of the International Committee of Military Medicine and Pharmacy, Colonel Voncken, Liège, Belgium, before April 1, 1940. The eleventh congress will be held in Switzerland in 1941.

Government Services

Cancer Institute Lends Radium

Hospitals in twenty states and the Territory of Hawaii will shortly receive loans of about 8.5 Gm. of radium from the National Cancer Institute, the U. S. Public Health Service has announced. The radium is now being tested by the U. S. Bureau of Standards and prepared for shipment in specially constructed lead containers. In approving applications, the officials of the institute made their choices on the basis of need for radium and the competence of staff and adequacy of facilities for radium treatment. The institute still has about 1,300 mg. of radium that has not been allotted and applications will continue to be received. Institutions receiving the loans must agree to make no charges to the patients for its use and must meet high standards regarding personnel administering the treatment.

Physicians Wanted for CCC Duty

Vacancies exist in the CCC in the Eighth Corps Area wherein the services of physicians can be utilized as civilian employees (physicians) or as contract physicians. Applicants should be graduates of class A medical schools and should address their applications to The Surgeon, Headquarters, Eighth Corps Area, Fort Sam Houston, Texas. Consideration will be given to applicants, as follows:

1. Medical reserve officers in the grade of captain or above who are eligible for active duty and promotion. They may be placed on duty under classification P-3 at the initial rate of pay of $3,200 a year.
2. Medical reserve officers in the grade of first lieutenant, if qualified, may be placed on duty under classification P-2 at the initial rate of pay of $2,600 a year.
3. Physicians who are not members of the medical reserve corps can be placed on duty as contract physicians at the initial rate of pay of $2,600 a year.

All the candidates must consider themselves physically qualified and, if selected, must report to their first place of assignment at their own expense, and if found physically qualified they will be appointed at the respective rates. If on being relieved from duty, either at the request of the individual or for the convenience of the government, the return transportation must also be at the expense of the individual.

Foreign Letters

LONDON

(From Our Regular Correspondent)

July 15, 1939.

Injection of Pituitary Extract Immediately After Delivery

At the Section of Obstetrics and Gynecology of the Royal Society of Medicine, the effects of injecting pituitary extract immediately after delivery were discussed. Mr. S. G. Clayton tested the effects of injecting 5 units of solution of posterior pituitary immediately after delivery in eighty-three primigravidas and thirty-four multigravidas. He found that the duration of the third stage was slightly reduced—from an average of 16.7 minutes in primigravidas used as controls to fifteen minutes, and from 13.2 to 9.9 minutes in multigravidas. Then the amount of bleeding was investigated. In 117 test cases five showed a loss of more than 20 ounces (600 cc.), an incidence of 4.2 per cent, while in controls the figure was 3.8. Manual removal of the placenta was required five times in 372 control cases (three for hemorrhage, two for retained placenta); in 117 test cases it was required three times and in two retention was attributed to hour-glass spasm of the uterus. One primigravida was normally delivered after thirty hours' labor. Five units of solution of posterior pituitary was immediately given. After fifty minutes the placenta was still retained in spite of repeated attempts at expression and saline injection of the umbilical vessels. As slow loss continued, manual removal was attempted and a definite ring prevented passage of the hand until amyl nitrite was given and relaxed the ring. A second primigravida required similar treatment.

Mr. Clayton drew the following conclusions: 1. Solution of posterior pituitary slightly lessened the average duration of the third stage. 2. The incidence of postpartum hemorrhage was not reduced. 3. There is danger of hour-glass spasm of the uterus, with the ensuing risk of manual removal of the placenta. 4. It seems unjustifiable to expose the patient to this risk for the doubtful advantage of shortening the third stage.

In the second paper Mr. Clayton's conclusions were endorsed and in addition more than doubling of the incidence of postpartum hemorrhage was noted in the pituitary cases. But in the third paper this incidence was stated to be diminished and no tendency to a contraction ring was found.

Lord Horder Recommends Coeducation

In this country the rule, with very few exceptions, is to educate boys and girls in different schools, but Lord Horder, speaking on Parents Day at Bedale's School, Petersfield, Hants, one of the few schools where coeducation is practiced, recommended this system. His ideal school was one that would give the essential foundation of self discipline, good manners, cleanliness and punctuality. He would not bother so much about academic training. Nobody bothered about his. But he would bother about health, about food and more about rest to both body and mind. He would bother also about possibilities for manual work, some chance of close contact with the good earth. "I see in my consulting room the effects of coeducation as well as the effects of the lack of it. I think that coeducation is the natural thing, just as I think that the separate education of the sexes is the artificial thing. There must be, at least for the only child, great advantages in coeducation. For the children of families where the sex is the same the advantage of coeducation is also obvious. I have met in after-life those who had received the benefits of coeducation. I did not find that the boys were effeminate or the girls unfeminine."

Euthanasia Again Debated

Euthanasia, the right to die when suffering from painful incurable disease, is a subject of perpetual controversy. It is not legal for a physician to give a drug with lethal intent even at the request of the patient, and a bill to legalize euthanasia was recently defeated in the House of Lords. The subject has been debated from time to time at medical meetings but not at a public meeting such as has just taken place under the chairmanship of Mr. Neville Laski, a lawyer. The case for euthanasia was stated by Sir James Purves-Stewart, neurologist. He referred to a woman friend, suffering from a painful disease, who asked for something to make her sleep and never wake. "I will not say what action I took," he said, "but next day she failed to wake." "Some people charge us with murder," he continued. "I have received abusive letters to that effect, but murder is killing with malicious intent whereas voluntary euthanasia is an act of mercy. Individuals should be permitted to substitute a painless death for a slow and painful one. We do not propose that doctors would be allowed to kill all patients with incurable diseases." A Roman Catholic speaker said that the bill to legalize euthanasia was full of criminal possibilities. He doubted whether a man's will could be said to be sound when very ill and asked to sign a paper for euthanasia. It was usurping the prerogative of God. Sir Arnold Wilson, M.P., was not satisfied that in the words of Christ there was anything definite against euthanasia. Dr. Halliday Sutherland said that he knew of no instrument for judging pain like the thermometer which measured temperature. Pain was relative and in his experience Northern races of Europe suffered pain better than the Southern, and woman better than man.

When Purves-Stewart rose to reply there was an uproar in which cries of "Murder" were heard. He referred to the case of four men brought to a hospital scalded by a boiler explosion. When an attempt was made to take off their clothes the skin came away, exposing the muscles twitching all over the body. Their tongues and nostrils were so swollen that they could hardly breathe. "We gave each a huge injection of morphine and did not measure the quantity. Three died an hour later and the other in four hours. Was that a crime or an act of mercy?" A roar of conflicting answers came from the meeting. Summing up, Mr. Laski said that under the present law euthanasia was murder. "If this bill ever becomes law, I am not going to be one of the signatories."

The Shortage of Nurses and War Services

In the House of Commons a medical member, Sir Francis Edward Fremantle, called attention to the inadequate supply of nurses; 20,000 entrants to the profession were required yearly but only 12,000 were obtained. The long hours of work constituted the chief difficulty. Nurses of all grades suffered under a constant strain. Most hospitals were trying to reduce hours but were handicapped by a scarcity of recruits. The ninety-six hour fortnight was the utmost that could be achieved in the near future. Dr. Elliot, minister of health, said that the shortage arose from an increased demand; the number of nurses qualified annually had risen in ten years from 6,000 to 10,000. Many of the accusations about the conditions of service were exaggerated, but there was still scope for improvement.

WAR SERVICES

An important part of the subject was the aspect of war services. With regard to hospital bed expansion in time of war, in Great Britain 200,000 beds would be available in the first twenty-four hours. There would be beds in existing institutions for which a nursing staff was already provided. In addition, 100,000 beds were to be added to existing hospitals for which the staff was not at present provided. Nurses and auxiliaries were also needed for first aid posts and for those millions of children and others to be evacuated from populous areas. The government was therefore asking for 100,000 volunteers. It wanted the big organized units of industry to give facilities to their staffs for training. He also appealed to retired trained nurses to register with the central emergency committees. There had already been substantial recruitment of Red Cross nurses, and some 7,000 untrained young women were undergoing training for qualification as nursing auxiliaries. But many more were required and he appealed to women to come forward.

Blood Donors In and Around London

This country has never been prepared for war in time of peace on any such scale as at present. The defense of the civil population against air raids is a new and immense problem. The blood transfusion service is a remarkable example of what is being done. At seventy centers throughout the country volunteers are being tested for their suitability as blood donors. All healthy men and women between the ages of 21 and 65 who are likely to be available at least during the early part of a war are asked to volunteer. Already more than 10,000 have been tested in the London area. For the center of London alone 100,000 volunteers are needed, and 250,000 for Greater London and the surrounding country. In the event of food becoming scarce, donors will be given extra rations to maintain the quality of their blood. After testing, donors are given a distinctive card stating to which of the four groups their blood belongs, so that in an emergency they will know where to report. Depots for the cold storage of blood, each equipped with at least 10,000 bottles and apparatus for its collection and distribution, have been arranged. The institution of these depots is based on experience in the Spanish war, in which Jorda's institute in Barcelona was a remarkable success. It was found that at least 10 per cent of the casualties could be saved by blood transfusion.

Henry Havelock Ellis

Henry Havelock Ellis, philosopher, critic and essayist, known the world over for his writings on sex and its aberrations, on which he was the first to write systematically in English, has died at the age of 80. An East Anglian, the son of a sea captain, much of his childhood was spent at sea. At 15 he went for his health in his father's ship to Australia, where he taught in various schools. In the solitude of the bush he passed through unhappy periods of storm and stress and decided that he would devote his life to elucidating the obscure problems of sex. For this purpose he returned to England and studied medicine at St. Thomas's Hospital. He qualified in 1889 at the age of 30. He practiced medicine for only a few months and gave himself up to literary work, in which he had been engaged even when a student. He edited the Contemporary Scientific Series, in which some important works appeared for the first time in this country. Among other books from his pen were A Study of British Genius, The Philosophy of Conflict, The Criminal, The Task of Social Hygiene and The Problem of Race Degeneration. His Studies in the Psychology of Sex appeared in 1898 but was not completed until 1910 and supplementary volumes appeared in 1928. In spite of protests from the medical press, it was suppressed by the government as obscene and he transferred its publication to an American publisher in Philadelphia. The work is now recognized as in the first scientific rank and to it is due most of the modern freedom of discussion of sex matters. He maintained that "we can never learn to reverence life until we know how to understand sex" and it is largely due to his teaching that sexual perversion is no longer regarded

V 19

as simply a matter of depravity but as a morbid phenomenon to be studied. An earlier book, The New Spirit (1890), emphasized the importance of sex in human affairs. Man and Woman (1894) was a study of human secondary characteristics and an introduction to a more elaborate investigation. Ellis was an idealist to whom money was a secondary consideration. It was only comparatively late in life that he received more than a bare living from the sale of his books. He was shy and retiring and never appeared in public or lectured.

PARIS

(From Our Regular Correspondent)

July 1, 1939.

Tuberculosis Among Physicians and Nurses

The results of the tuberculin test in medical students and in student nurses have shown that the epidemiologic picture has been modified since the beginning of the century; 40 per cent of the recruits reporting for military training in France and 25 per cent of the students enrolling for medical studies have a negative cutaneous reaction. Rist has set forth before the Academy of Medicine statistics gathered by Heinbeck of Oslo and those of his own in the nurses' schools of the hospitals of Paris. Fifty-eight per cent of the members of one class numbering 144 and watched for two years showed a positive cutaneous reaction on entering. None of these had any trouble with their health while they were at school. Of sixty others, forty-four gave indication of change in the reaction; 10 per cent of these had a clinically proved tuberculosis, and one of them died. In the complete personnel of the Paris hospitals in which Rist has charge of matters pertaining to tuberculosis, 0.65 per cent (in 1931) were tuberculous, a figure reduced for 1938 to 0.37 per cent. Accordingly, the morbidity of the personnel constantly in contact with germ carriers is thirty times less than that of nurses in training. There is therefore an enormous difference between the risks of first year nurses with an allergic reaction and those with a negative cutaneous reaction.

How can one protect these young student nurses? Give them the allergic protection which they need by immunization with BCG vaccine. Heimbeck, who has employed this method, has ascertained that morbidity and mortality from tuberculosis were ten times less among nurses vaccinated and immunized than those not vaccinated. Since there still exists distrust against BCG inoculation, one must begin by recommending vaccination to nurses in training with a negative cutaneous reaction; compulsion may be considered subsequently. This vaccination should be parenteral by intradermal injections. It is strictly contraindicated in patients either allergic or in process of being rendered allergic.

Medicolegal Lecture on Blood Stains

At the last meeting of representatives of medical jurisprudence in Paris, Balthazard pointed out the conclusions which can be drawn in cases in which blood is projected on the ground, on walls or on other surfaces. He has confined his research to the laws by which stains left by blood are regulated. His technic consists in causing drops of blood to fall on different surfaces from varying heights and angles. These experimental studies are supplemented by cinematographic observations of the emission of the blood drops. Bull's electric spark process allows 500 photographs to be taken in a second during a period of time which cannot exceed one tenth of a second.

For drops falling on horizontal surfaces the problem is: Can one determine the height of the fall from the appearance of the drop? If the drop falls from a very low height, the stain is circular. If it falls from a considerable height, points appear on the periphery. The number of these points depends on the height of the fall but still more on the volume of the drop of blood. The length of the points furnishes information of only a small degree of precision. Apart from the stains, more or less numerous jets can be observed; but neither their number nor their distance from the main body of the stain nor their volume yields indications of practical use. In criminal practice the most frequent type of blood stains are those which strike the surface on which they are observed obliquely. The stains lengthen out in proportion as the angle at which they strike is acute. The angle at which the drops fall is determined with great exactness by the relations between the length and breadth of the stain. Examination of the base of the stain reveals the height of the fall. Drops that fall from a height have a lengthened base like that of a brush. Stains are not homogeneous, especially if they are old. A crust formed at the lower end, becoming increasingly dark, may indicate the age of the stain.

The cinematographic examination of the fall of drops of blood has offered data on how to distinguish stains according to the origin of the blood; whether, for example, the blood comes from a wound or has been expectorated. In the same way, research has been made on how the appearance of a stain changes according to the object which the blood strikes (wall, paper, cloth). The problems are rendered complex by considerations such as adherence, lack of impregnation of the paints, fabric or paper, absence of expansion, variation in the spread according to the grain of the cloth, paper and felt, the contraction and desiccation of projected blood and the source of the projected blood (corpse or living person). The illustrations accompanying the paper of Balthazard and his collaborators may be exceedingly useful in medical jurisprudence.

Professional Guidance

France is a country of great individual liberty. Every one recognizes the importance of vocational orientation, but every one refuses to submit to constraint. Politics undertook to impose state control, but the reforms did not gain popularity. French parents will not admit that the state has all rights over their children. Neither did the French medical profession receive professional guidance sympathetically. One had no confidence in the technics of professional guidance, because of the enthusiastic assertions of their inventors. Hilaire, assistant general secretary of the confederation of French medical councils, presented the medical points of view before a recent meeting at the Institute of Professional Orientation. It is to the school physician who has received the necessary training that one must entrust the care of advising parents regarding the aptitudes of their children, what risk they incur in certain callings and the disappointments awaiting them in callings for which they are not adapted. The family physician can cooperate in this guidance by furnishing any information on the child which he has.

Institute of Cancer Research

An institute of cancer research was recently opened in North Lille. This is not a therapeutic center but has for its object the bringing together of all research activities. It is open to all research scientists, who will find in three kinds of laboratories (histophysiologic, chemical and physical) perfect equipment and a perfectly coordinated mechanization to aid them. The principle stressed is team work. This institute was created with subsidies received by Mr. Herbert Hoover and with the remainder of the funds of the American Committee for the Aid of Liberated Regions and of the Committee for Relief in Belgium.

BERLIN

(From Our Regular Correspondent)

July 3, 1939.

News of the Universities

Secretary of education Rust has made a speech sketching the future inner construction of the universities. He never spoke more clearly. A problem of the universities found expression in the demand for shortening the period of academic study, as this previously has been done in case of medical students. The universities should now revise all their activities, including the plan of study. The laying aside of final examinations should be a temporary expedient. This the secretary admitted publicly. General exemption from school fees in the higher grades (i. e. gymnasiums) is not yet practicable. Secretary Rust pointed furthermore to the necessity of closer ties between scientific preparation and practical training; in order to gain time the practical training should be done, partly at least, at the time of theoretical studies. The secretary believes that through variety created thereby also better results in studies could be obtained. Abbreviation of the duration of studies would place higher requirements also on the professors; they should observe the students in person to form an opinion of them. In such situation, said the secretary, the university professors should think less for once of their publications and more of the living body of men, as he expressed himself. The university professor should resolve now to be a teacher first of all (that is, not a researcher).

As the result of the lack of aftergrowth, with which all these efforts are concerned in the long run, one should act in three ways: (1) abbreviate the years of study, (2) prolong the duration of semesters and (3) connect more closely theoretical and practical training. The conference of rectors laid down finally twelve "points for the task of the German universities," which however contain nothing not generally known or not contained in the preceding parts. Two points read: "The fulfilment of the national tasks set for German science does not encroach on the freedom of instruction and research, which is an essential characteristic and solid foundation of the German university and of its idea of science." "The national socialist German university shall be the institution of higher learning of the German people." These two points are sufficiently characteristic. In this connection an utterance of the national student-leader, Dr. Scheel, is of interest. He has an influential position in university circles; he announced before 700 student subleaders that the national student council reserves its decision on the final form of the German university. Indeed, one has to consider that universities and intellectual life cannot be changed as rapidly as other fields. He gave clear warning, on the other hand, that the students could eventually look for their education at places other than the universities, for instance at the so-called castles of order, i. e. subleader training establishments of the national socialist party. The national student-leader actually said this. In the future admission will be possible only through selection undertaken by the party. Furthermore, Dr. Scheel was in favor of German students studying abroad. He added that the students one encounters today at some foreign universities as representatives of the German student body are unsuited to represent the national socialist deportment and conception of the world. Therefore the number of German students abroad should be greatly increased.

The regulation of formal admission of an academic lecturer into a faculty has already acquired a new form. The economic situation and the absence of aftergrowth of university professors as well as the new conditions created by the annexation of Austria and the Sudeten territory prompted the secretary to take these measures. The regulations concerning the obtaining of a teaching post have undergone several important changes also as regards the economic security of the teachers. The obtaining of the teaching post is connected, besides the previous acquisition of the title "Dr. habil.," with successful participation at a course of the national camp for functionaries. In case the dean granted the admission to public trial-instruction, the candidate has to make three one hour lectures on three different days pertaining to his field of specialization; the subject of the lecture is chosen by the dean. This nearly corresponds to the procedure followed up to the present. In case of favorable decision, the secretary of education having the sole right to decide, with the appointment as a teacher (as up to the present), the candidate is admitted to the status of functionary at the same time; this is new and is valuable economically to the young teachers. The teacher who formerly had no claims for compensation for his teaching activity in Germany outside some income from lectures (mostly an insignificant amount) becomes a functionary. The secretary can appoint as extraordinary professors teachers who distinguished themselves in instruction and research; this appointment however does not establish any claim on the state and especially does not justify any expectancy of a full professorship. The authorization to teach, which is conferred exactly defined, that is limited to a definite branch of medicine, can be broadened with the consent of the secretary; it can also be restricted by the secretary in the interest of the university. An eventual changing of the university requires the consent of the secretary. According to this new regulation all teachers appointed heretofore and extraordinary professors not in office have to make a motion for appointment; should they fail to do this, they lose their teaching authorization as of Oct. 1, 1939.

The position of honorary professor was also defined in a recent decree of the secretary of education. Honorary professorship is not a title, it is an academic distinction. Scholars who do not belong to the teaching staff of a scientific institution of higher learning can be appointed honorary professors. They must be able to cooperate in the instruction and research problems of the faculty in conformity with their scientific accomplishments and meet the requirements of holders of academic professorial chairs. There is no admission to the status of functionary connected with the appointment by the secretary of education. The appointment does not create an employment relationship with the state and does not establish claims on the state, particularly for a university professorship. The appointment is valid as long as the appointee belongs to the teaching staff of the university. At the end of his sixty-fifth year the honorary professor needs the consent of the rector to continue his teaching activity. There are only a few honorary professors at the various faculties of medicine—mostly well known researchers in their fields. In the last years occasionally political considerations had their share in the appointment.

The question of academic aftergrowth is causing more and more concern. There often is a lack of appropriate persons to fill important professorial chairs. The gap created through the elimination of so many university professors by the well known proceedings of the last years cannot be filled by the present management of the German universities. A recent book gives a typical example of this exigency, as in case of university professors of law, of no special importance however. The author of this book, entitled "The German Professor of Law," is Professor Kisch, holder of a professorial chair at the Faculty of Law of the University of Berlin and in no way opposed to the present government. What he has to say therefore appears so much more significant. He speaks of "the very serious turn" of the problem of aftergrowth of university professors in the last years. There is a shortage of candidates and at times the quality of aftergrowth leaves much to be desired. It is quite difficult, in many cases impossible, to find suitable talent for vacancies of professorial chairs. The faculties of law supposedly

do not display any more the high quality they used to display. This situation is the result of the attitude of many influential groups with regard to university professorships. It is furthermore the result of the method of selecting the young aftergrowth, in which political considerations also take part. Hence the future university teachers have to attend a training camp for functionaries and "prove themselves" there, before they are appointed. In this connection the president of the national board of bar examinations also complained about the failures at the final examinations of legal studies and observed a "deplorable lack of knowledge" in the most important fields—a complaint already voiced by this office. This also is generally characteristic. Many of these claims are perhaps more easily understood in case one knows how higher government circles think about it. The secretary for propaganda, Dr. Goebbels, published an article recently under the title of "The Intellectual" in which he explained the notion of "intellectualism." To quote a few passages for the sake of illustration: "An intellectual is a man in whom civil valor is in inverse ratio to knowledge acquired through studies. . . . This intellectual is in reality an artificially highly bred accumulation of knowledge. . . . These men represent to quite an extent those who said 'no' to national socialism and to the work of the 'Führer' (leader) at every election. . . . There is no place in their black hearts for a great warm political passion." And the national student-leader, Dr. Scheel, recently said the following concerning the building up of student aftergrowth: "The aim is to produce a new type, separated by a world from a former flabby intellectualism." After taking note of these utterances coming from authoritative sources, one understands better perhaps some of the proceedings and complaints concerning the universities—and naturally this concerns the physicians.

BUENOS AIRES

(From Our Regular Correspondent)

July 15, 1939.

Hypertension and the Ischemic Kidney

Drs. Braun Menéndez and Fasciolo are carying on some experiments started by Drs. Houssay, Fasciolo and Taquini. They experimented with the ischemic kidney in three conditions: (1) diminishing the lumen of the renal artery of a kidney which was transplanted to the neck of a dog, (2) also diminishing the lumen of the renal artery of a kidney which was irrigated with blood and (3) inducing total occlusion of the renal artery. It was verified in three cases that the kidney which has either an incomplete irrigation or is not irrigated at all produces a hypertensive and vasoconstrictor substance which passes into the blood. The truth of the statement is verified by three facts: (1) The transplantation of the kidneys in the neck of a normal dog induces a rapid increase of the arterial pressure of the animal, (2) the venous renal blood taken from the animal during the period of diminution of circulation and perfused through the surviving isolated circulatory system of a toad produces vasoconstriction and (3) if ischemia is done in such a manner as to permit the passage of 8 or 10 cc. of blood for each minute, and 100 cc. of the blood is collected during ten or fifteen minutes and given to a dog by intravenous injection during two or three minutes, the blood pressure of the dog increases. If the injection is done with venous blood of a kidney which is not in ischemia or else with carotid blood or with jugular venous blood, the blood pressure of the animal slightly increases. The results of the experiments prove that the ischemic kidney produces a hypertensive substance.

Diminution in Birth Rate

The birth rate in the population of Argentina shows a progressive diminution. It diminished from 39 in 1911 to 24 in 1937. The diminution is not due to economic factors, as it is observed mainly in well-to-do families. Social and moral reasons are the main factors. Luxury and the demands of modern life are the causes for which conception is prevented. Several projects have been presented to the congress with the aim of establishing laws by which the birth rate may be stimulated and the families with children given economical remunerations.

Prevention of Goiter

Two bills have been presented before the house of senators for organizing a crusade against endemic goiter in Mendoza Province. In one of the bills there is an early allowance of 1,000,000 Argentine pesos ($250,000) and 500,000 pesos ($125,000) a year. In the other bill the figures for prevention of goiter and other work for sanitation of the province make an amount of 8,000,000 Argentine pesos ($2,000,000).

Personals

Dr. A. H. Roffo was presented with the Amerongen prize, which was established for the production of cancer by feeding. Dr. Roffo had presented the results of the production of gastric cancer in rats. The animals had a diet of milk and bread, besides irradiated yolks of eggs, irradiated cholesterol and boiled lard and beef suet.

Dr. C. Fonso Gandolfo was appointed professor of infectious diseases at the Faculty of Medicine of Buenos Aires.

The Liga Francesa contra el cancer awarded the Amerongen prize to Dr. H. Roffo for his work on provocation of cancer from food in rats.

Profs. A. Sordelli and B. A. Houssay have been given the title of Officer of the Legion of Honor by the French government.

Deaths

Dr. Manuel Battaglia, secretary of the national department of hygiene of Buenos Aires, died February 23 of pulmonary edema.

Dr. Antonio A. Martínez, professor of pediatrics of the Faculty of Medicine of Buenos Aires, died January 19.

Marriages

WILLIAM CESYL BUSS, Bakersfield, Calif., to Miss Dorothy E. Hannon of Sunbury, Pa., at Pixley, Calif., recently.

WALKER THOMPSON, Iowa City, to Miss Mary Martha Gordon, formerly of Houston, Texas, March 11.

HAROLD PAGAN HOPE to Miss Helen Jeter Hamilton, both of Union, S. C., at Columbia, June 22.

ROBERT SPENCER HOWELL, Miami, Fla., to Miss Mary Louise Mullino of Montezuma, Ga., June 7.

LAWRENCE E. GEESLIN to DR. AMELIA BURNS SHEFTALL, both of Augusta, Ga., recently.

CHARLES W. IHLE JR., Cleghorn, Iowa, to Miss Helen Louise Hackett of Pittsburgh, July 1.

WILLIAM E. MOORE, New Haven, Conn., to DR. MARGARET I. HYDE of Baltimore, June 6.

GARTH EDMUND FORT, Nashville, Tenn., to Miss Chloe Frierson of Columbia in June.

CHARLES F. OWEN JR., Canton, N. C., to Miss Eloise Harnden of Philadelphia, July 10.

JAMES MYERS HICKS, Florence, S. C., to Miss Welker Delle Sellers of Mullins, June 15.

DAVID P. FINDLEY, Omaha, to Miss Lenore Hanson at Oconomowoc, Wis., April 22.

THEODORE SIDNEY RAIFORD to Miss Ann Irish, both of Decatur, Ill., June 20.

HENRY F. HALL JR., Columbia, S. C., to Miss Mary Hennies of Chester, July 4.

LEON HOSKINS, Harlan, Ky., to Miss Lida Lee Atkins of Pineville in June.

DAVID SCHREIBER to Miss Leah Cohen, both of New York, June 22.

Deaths

Frederick Parker Gay ● New York; Johns Hopkins University School of Medicine, Baltimore, 1901; an Associate Fellow of the American Medical Association; secretary of the Section on Pathology and Physiology, American Medical Association, 1914-1916; professor of bacteriology, Columbia University College of Physicians and Surgeons, New York, and formerly professor of bacteriology at the University of California Medical School, Berkeley; assistant and instructor in pathology at the Harvard Medical School, Boston, 1907-1910; member of the Association of American Physicians, American Association of Pathologists and Bacteriologists and the American Society for Experimental Pathology; served during the World War; member of the medical section of the National Research Council, 1917-1924, chairman in 1922 and chairman of the medical fellowship board, 1922-1926; was exchange professor at Belgian universities in 1926; author of "Studies in Immunity," 1909, "Typhoid Fever," 1918, and "Agents of Disease and Host Resistance," with others, 1935; contributed to scientific journals on bacteriology, immunology and pathology; aged 64; died, July 14, in New Hartford, Conn.

Stephen John Maher ● New Haven, Conn.; Yale University School of Medicine, New Haven, 1887; past president of the Connecticut State Medical Society and the New England Conference on Tuberculosis; member of the Society of American Bacteriologists; for many years member of the board of the National Tuberculosis Association, and chairman of the State Tuberculosis Commission; was an official representative of the United States government at the International Tuberculosis Conference in Rome in 1928, Sweden in 1930, Lausanne in 1924, Amsterdam in 1932 and Lisbon in 1937; in 1932 received the Laetare Medal from Notre Dame University, South Bend, Ind.; for two years member of the city board of health; consulting physician to the Hospital of St. Raphael; member of the board of directors of the Gaylord Farm Sanatorium, Wallingford; aged 79; died, June 7.

Henri A. Lafleur, Montreal, Que., Canada; McGill University Faculty of Medicine, Montreal, 1887; emeritus professor of medicine at his alma mater; member of the Association of American Physicians; was president and for many years member of the Medical Council of Canada; formerly vice president of the College of Physicians and Surgeons of the Province of Quebec; consulting physician to the Grace Dart Home Hospital and the Montreal General Hospital, where he died, June 4.

Ernest Cooper ● State Park, S. C.; Johns Hopkins University School of Medicine, Baltimore, 1910; vice president of the South Carolina Tuberculosis Association; for many years superintendent of the South Carolina Sanatorium; formerly member of the board of directors of the National Tuberculosis Association; aged 62; died, May 6, at the Columbia (S. C.) Hospital of cardiovascular disease and bronchopneumonia.

Ova Portia Davis, Topeka, Kan.; University Medical College of Kansas City, Mo., 1896; Bellevue Hospital Medical College, New York, 1897; member and past president of the Kansas Medical Society; past president of the Shawnee County Medical Society; formerly professor of principles and practice of medicine at the Kansas Medical College; on the associate staff of the Christ's Hospital; aged 69; died, May 28.

Robert Drane Jewett, Wilmington, N. C.; University of Virginia Department of Medicine, Charlottesville, 1888; member, and secretary 1893-1898, of the Medical Society of the State of North Carolina; owned and edited the *North Carolina Medical Journal*, 1892-1898; aged 79; died, May 6, in the James Walker Memorial Hospital of lobar pneumonia.

Gilbert Royce, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1897; formerly professor of otolaryngology at his alma mater; fellow of the American College of Surgeons; served during the World War; on the staffs of the Victoria Hospital for Sick Children and the Toronto General Hospital; aged 69; died, May 23.

Archer Dorval Babcock, Syracuse, N. Y.; University of Buffalo School of Medicine, 1893; member of the Medical Society of the State of New York; served during the World War; on the staff of the Crouse-Irving Hospital; aged 69; died, May 25, of cerebral thrombosis, chronic endocarditis and coronary infarction.

Albert Fay Lowell ● Gardner, Mass.; University of Vermont College of Medicine, Burlington, 1900; fellow of the American College of Surgeons; attending surgeon to the Henry Heywood Memorial Hospital, Gardner (Mass.) State Hospital and the Peterboro (N. H.) Hospital; aged 63; died, May 14, of pneumonia.

Samuel Harris Newman, Dadeville, Ala.; Memphis (Tenn.) Hospital Medical College, 1898; member of the Medical Association of the State of Alabama; past president of the Tallapoosa County Medical Society; at various times member of the local school board and city council; aged 71; died, May 19, of myocarditis.

Chester Harris Sample, Saginaw, Mich.; Bellevue Hospital Medical College, New York, 1874; member of the Michigan State Medical Society; fellow of the American College of Surgeons; past president of the Saginaw County Medical Society; surgeon to St. Mary's Hospital; aged 88; died, May 3, of senility.

Rollin Roy Nevitt ● Moran, Kan.; Kansas City (Mo.) Homeopathic Medical College, 1896; past president of the Allen County Medical Society; served during the World War; aged 69; died, May 14, in the Mercy Hospital, Fort Scott, following a cholecystostomy, cholelithiasis and postoperative pneumonia.

Arthur Edward Williams, Rock Island, Ill.; Northwestern University Medical School, Chicago, 1902; member of the Illinois State Medical Society; past president of the Rock Island County Medical Society; aged 63; on the staff of St. Anthony's Hospital, where he died, May 25, of heart disease.

Claude Carl Lytle ● Geneva, N. Y.; Syracuse University College of Medicine, 1900; fellow of the American College of Surgeons; for several years member of the board of health; attending surgeon to the Geneva General Hospital; aged 65; died, May 3, of diabetes mellitus and coronary embolism.

James Lewis Pierce, Marianna, Fla.; Emory University School of Medicine, Atlanta, 1926; member of the Florida Medical Association; formerly secretary of the Jackson County Medical Society; aged 38; was killed, May 27, in an automobile accident near Thomaston, Ga., en route to Atlanta.

David McClurg, Detroit; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1892; member of the Michigan State Medical Society; on the staff of the Highland Park (Mich.) General Hospital; aged 74; died, May 25, of hypertension and coronary occlusion.

Edward Francis Day ● Binghamton, N. Y.; University of the City of New York Medical Department, 1895; on the staffs of the Binghamton City Hospital and Our Lady of Lourdes Memorial Hospital; aged 67; died, May 18, of chronic arthritis, aplastic anemia and ulcerative colitis.

James F. Roseborough, Marshall, Texas; Tulane University of Louisiana School of Medicine, New Orleans, 1893; member of the State Medical Association of Texas; past president of the Harrison County Medical Society; aged 83; died, May 13, of coronary thrombosis.

Millard Percy Doyle, Norfolk, Va.; Medical College of Virginia, Richmond, 1907; member of the Medical Society of Virginia; on the staffs of the Norfolk General Hospital, Leigh Memorial Hospital and St. Vincent's Hospital; aged 58; died, May 8, of coronary occlusion.

Henry Chilton Osborn, Ashland, Ky.; University of Louisville Medical Department, 1910; member of the Kentucky State Medical Association; served during the World War; on the staff of the King's Daughters' Hospital; aged 56; died, May 6, of a cerebral hemorrhage.

James A. Reeder, Clare, Mich.; Detroit College of Medicine, 1898; member of the Michigan State Medical Society; owner of the Clare Hospital; formerly coroner and health officer; aged 76; died, May 7, in the Harper Hospital, Detroit, of Hodgkin's disease.

Coalby T. Rives, Winters, Texas; College of Physicians and Surgeons, Little Rock, Ark., 1911; member of the State Medical Association of Texas; past president and secretary of the Runnels County Medical Society; aged 65; died, May 14, of chronic nephritis.

Joseph Aloysius Dillon ● New York; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1894; served on the staff of the New York Foundling Hospital in various capacities; aged 69; died, May 3, of angina pectoris.

Harold Fredrich Neilsen, Minneapolis; University of Minnesota Medical School, Minneapolis, 1930; member of the Minnesota State Medical Association; formerly deputy coroner; aged 34; died, May 23, in the Swedish Hospital of pulmonary tuberculosis.

Joshua Milburn Dougherty Jr. ● Gate City, Va.; Medical College of Virginia, Richmond, 1925; secretary of the Scott County Medical Society; on the staff of the Holston Valley Community Hospital, Kingsport, Tenn.; aged 38; died suddenly, May 4.

Alfred Raymond Lozano, Montgomery, Ala.; Université de Paris Faculté de médecine, France, 1932; member of the Medical Association of the State of Alabama; aged 34; died, May 18, in Corpus Christi, Texas, of carcinoma of the tongue.

Henry G. B. Nixon ● Hartland, Wis.; Detroit College of Medicine, 1887; bank president; formerly on the staffs of the Municipal Hospital, Waukesha, and the Summit Hospital, Oconomowoc; aged 73; died, May 19, of coronary thrombosis.

Francis Albert Hargrave, Palo, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1884; member of the Michigan State Medical Society; for many years member of the school board; aged 82; died, May 6.

Jay O. Spinning, Litchfield, Mich.; Hahnemann Medical College and Hospital, Chicago, 1876; aged 86; died, May 28, in the James W. Sheldon Memorial Hospital, Albion, of pulmonary infarction following a cystotomy, and prostatism.

Charles Fernando Myre, Chippewa Falls, Wis.; School of Medicine and Surgery of Montreal, Que., Canada, 1899; aged 66; on the staff of the Northern Wisconsin Colony and Training School, where he died, May 5, of chronic myocarditis.

William John Scott, Cookstown, Ont., Canada; University of Toronto Faculty of Medicine, 1918; served during the World War; aged 44; died, May 7, of injuries received when he fell from the fifth floor balcony of a hospital in Toronto.

Charles Spurgeon Strain, Rochester, Mich.; Detroit Homeopathic College, 1902; member of the Michigan State Medical Society; served during the World War; aged 68; died, May 16, in a hospital at Pontiac of heart disease.

William R. Hand, Fargo, N. D.; Cincinnati College of Medicine and Surgery, 1877; member of the Minnesota State Medical Association; aged 82; died in May of obstruction of the common duct, gallstones and myocarditis.

Albert Herrick Thornton, Edgemont, S. D.; State University of Iowa College of Medicine, Iowa City, 1898; medical director of the Edgemont Hospital; aged 64; died, May 22, of chronic myocarditis following a chordotomy.

William Claude O'Neal, Palmyra, Mo.; St. Louis University School of Medicine, 1904; member of the Missouri State Medical Association; aged 64; died, May 20, in the St. Elizabeth's Hospital, Hannibal, of myocarditis.

Albert K. Barrier, Rolling Fork, Miss.; Kentucky School of Medicine, Louisville, 1885; member of the Mississippi State Medical Association; formerly county health officer; aged 80; died, May 31, of Parkinson's disease.

Eli G. Alcorn, Columbus, Ohio; University of Louisville (Ky.) Medical Department, 1895; formerly coroner of Gallia County; at one time member of the board of education of Gallipolis; aged 94; died, May 1.

Benjamin Smith Parks, Parkersburg, W. Va.; Barnes Medical College, St. Louis, 1906; member of the West Virginia State Medical Association; aged 56; was found dead in his garage, May 19, of asphyxiation.

William George Zantiny ● Long Beach, Calif.; Cleveland College of Physicians and Surgeons, Medical Department Ohio Wesleyan University, 1908; on the staff of the Community Hospital; aged 61; died, April 12.

Webb Suter, Campbellsburg, Ky.; Hospital College of Medicine, Louisville, 1905; member of the Kentucky State Medical Association; aged 59; died, May 23, in the Kentucky Baptist Hospital, Louisville.

Francis S. Wildner, Poughkeepsie, N. Y.; Deutsche Universität Medizinische Fakultät, Prague, Hungary, 1906; member of the Medical Society of the State of New York; aged 58; hanged himself, April 30.

Wilfred Teller La Fortune, Fitchburg, Mass.; Baltimore Medical College, 1910; member of the Massachusetts Medical Society; served during the World War; aged 52; died, May 8, of coronary thrombosis.

Hugh John Duffy, Chicago; University of Illinois College of Medicine, Chicago, 1911; served during the World War; aged 50; on the staff of St. Francis Hospital, Evanston, Ill., where he died, May 8.

John Andrew Tomasi, Bennington, Vt.; Georgetown University School of Medicine, Washington, D. C., 1934; aged 32; died, April 27, in the Caverly Preventorium, Pittsford, of pulmonary tuberculosis.

Horace Luten, Fulton, Ky.; University of Louisville Medical Department, 1898; served during the World War; aged 65; died, May 11, in the Illinois Central Hospital, Paducah, of coronary occlusion.

William Robert Haslewood ● Austin, Texas; Louisville (Ky.) Medical College, 1898; superintendent of the Austin State School; aged 68; died, May 15, of carcinoma of the esophagus and mediastinum.

Oliver J. Paris, Graham, N. C.; Baltimore Medical College, 1897; aged 72; died, May 2, in the Piedmont Memorial Hospital, Greensboro, of strangulated hernia, chronic nephritis and myocarditis.

Harrie Abijah James, New York; University of the City of New York Medical Department, 1891; member of the Medical Society of the State of New York; aged 78; died, May 2, of heart disease.

Christopher Columbus Gleaves, Los Angeles; Northwestern Medical College, St. Joseph, Mo., 1889; University of California Medical Department, San Francisco, 1889; aged 77; died, April 12.

Terry Kinney, San Marcos, Texas; University of the South Medical Department, Sewanee, Tenn., 1895; member of the State Medical Association of Texas; aged 71; died, May 3, of heart disease.

Robert Ellsworth Van Wickle, St. Louis; University of Pennsylvania School of Medicine, Philadelphia, 1937; an intern at the St. Louis Maternity Hospital; aged 31; died, May 14, of heart disease.

Robert T. Prine ● Ripley, Ohio; Medical College of Ohio, Cincinnati, 1897; past president of the Brown County Medical Society; aged 63; died, May 27, of arteriosclerosis and chronic myocarditis.

Alfred W. Gross, Chattanooga, Tenn.; Chattanooga Medical College, 1903; member of the Tennessee State Medical Association; aged 58; died, May 22, in the Newell and Newell Sanitarium.

Charles Jerome Bright Cave, Garrison, Barbados, B. W. I.; American Medical Missionary College, Battle Creek, Mich., and Chicago, 1907; medical missionary; aged 59; died, May 19.

Jackson Brainard Pellet, Hamburg, N. J.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1871; aged 91; died, May 3, of heart disease.

Roche W. Hogeboom ● Springfield, Mo.; Rush Medical College, Chicago, 1897; fellow of the American College of Surgeons; on the staff of St. John's Hospital; aged 63; died, May 1.

Edson Carey Miller, Brookings, S. D.; Chicago Medical College, 1874; member of the South Dakota State Medical Association; aged 92; died, May 21, of cerebral hemorrhage.

Joseph F. Miller ● Palmer, Ill.; Missouri Medical College, St. Louis, 1889; for many years bank president; aged 82; died, May 6, in St. Vincent Hospital, Taylorville, of pneumonia.

Edward Bancroft Rogers ● Collingswood, N. J.; College of Physicians and Surgeons, Baltimore, 1903; aged 61; died, May 12, in the Cooper Hospital, Camden, of pneumonia.

Ernest Maynard Freeman, Redlands, Calif.; University of California Medical Department, San Francisco, 1893; aged 74; died, April 27, of coronary occlusion and hypertension.

Margaret Josephine O'Sullivan ● Omaha; University of Nebraska College of Medicine, Omaha, 1927; aged 37; died, May 2, in the Immanuel Hospital of carcinomatosis.

Tonnes O. Ries ● Luck, Wis.; Milwaukee Medical College, 1911; aged 59; died, May 28, in St. Croix Falls (Wis.) Hospital of injuries received in an automobile accident.

Carl J. F. Rochow ● Rock Island, Ill.; Rush Medical College, Chicago, 1903; aged 61; on the staff of St. Anthony's Hospital, where he died, May 11, of heart disease.

John Isaac Pratt, Port Arthur, Ont., Canada; University of Toronto Faculty of Medicine, 1895; L.R.C.P., London, M.R.C.S., England, 1902; aged 65; died, May 3.

Otto Clarke Dunsworth, Trenton, Texas; Tulane University of Louisiana School of Medicine, New Orleans, 1907; aged 68; died, May 8, of pulmonary tuberculosis.

Peter Conway Kelley, Grand Island, Neb.; Barnes Medical College, St. Louis, 1898; at one time member of the state legislature; aged 68; died, May 17, of heart disease.

James Rufus Brown, Spartanburg, S. C.; Baltimore Medical College, 1892; aged 71; died, May 25, in the Spartanburg General Hospital of cerebral arteriosclerosis.

Bertrand M. O'Brien, Danville, Ind.; St. Louis College of Physicians and Surgeons, 1903; formerly county coroner; aged 58; died, May 1, of pulmonary tuberculosis.

Robert River Robertson, Portsmouth, Va.; College of Physicians and Surgeons, Baltimore, 1887; aged 77; died, May 24, in the Norfolk (Va.) General Hospital.

Philip Henry Holmes, Tarpon Springs, Fla.; University of Illinois College of Medicine, Chicago, 1903; formerly a practitioner in Chicago; aged 69; died, May 5.

Ralph Vorhees Murray, Roanoke, Ind.; Jefferson Medical College of Philadelphia, 1904; served during the World War; aged 57; died, May 6, of angina pectoris.

Edward Gilbert Cox, Gilbertsville, N. Y.; Albany Medical College, 1893; for many years police surgeon in Albany; aged 71; died, May 5, of coronary thrombosis.

William M. Campbell, Tulsa, Okla.; Missouri Medical College, St. Louis, 1890; member of the Oklahoma State Medical Association; aged 77; died, April 21.

Frederic Leroy Kellogg, Boston; Bellevue Hospital Medical College, New York, 1889; member of the Massachusetts Medical Society; aged 71; died, May 2.

James H. Logan, Lebanon, Okla.; University of Tennessee Medical Department, Nashville, 1892; member of the Oklahoma State Medical Association; died in May.

Charles Catlin Partridge, Melrose, Mass.; University of the City of New York Medical Department, 1883; aged 80; died, May 29, of cerebral hemorrhage.

David Joseph Mahan, Santa Rosa, Calif.; University of California Medical Department, San Francisco, 1906; aged 62; died, April 29, of coronary occlusion.

H. Will Elders, St. Joseph, Mo.; American Medical College, St. Louis, 1894; aged 65; died, April 23, in a hospital at San Francisco of arteriosclerosis.

Domitilo Rodarte ● El Paso, Texas; Universidad Nacional Facultad de Medicina, Mexico, D. F., 1901; aged 65; died, May 31, of bronchogenic carcinoma.

Ralph McDaniel, Waco, Texas; University of Texas School of Medicine, Galveston, 1898; also a druggist; aged 68; died, May 9, of combined sclerosis.

Arden Pascal Kessler, Dayton, Ohio; Ohio Medical University, Columbus, 1893; aged 70; died in April of arteriosclerosis and cerebral hemorrhage.

May C. Walker, Santa Cruz, Calif.; Kansas City (Mo.) Hospital College of Medicine, 1886; aged 80; died in April of heart disease and arteriosclerosis.

Mary Elizabeth Bliss, Utica, N. Y.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1896; aged 70; died, April 24, of coronary thrombosis.

Emile Oswald Voyer, Los Angeles; Medical Department of Hamline University, Minneapolis, 1906; aged 64; died, April 13, of chronic myocarditis.

George Byron Hyde ● Wilmington, Vt.; Atlanta Medical College, 1890; served during the World War; aged 76; died, May 17, of coronary thrombosis.

Roy Samuel George, Atlanta, Ga.; Atlanta School of Medicine, 1910; aged 49; died, May 5, of acute dilatation of the heart and cirrhosis of the liver.

Samuel Peskin ● New York; University of the City of New York Medical Department, 1898; aged 65; died, May 22, of coronary artery thrombosis.

Herman L. Nietert ● St. Louis; St. Louis Medical College, 1889; member of the Missouri State Medical Association; aged 73; died, May 9, of pneumonia.

Frank S. Wright, Salmon, Idaho; Willamette University Medical Department, Salem, 1887; formerly state senator; aged 75; died, April 19, of senility.

McClelland Shellman, New York; University of Minnesota Medical School, Minneapolis, 1934; aged 30; died, May 5, in the Presbyterian Hospital.

Frederick Wach, Salt Lake City; Illinois Medical College, Chicago, 1908; aged 69; died, April 14, of myocarditis and hypertrophy of the prostate.

Frederick C. Crawford, Toledo, Ohio; Cleveland Medical College, 1897; aged 65; died, May 8, in Negley of otitis media and streptococcic septicemia.

William Warren Tooker, Wichita, Kan.; Fort Wayne (Ind.) College of Medicine, 1891; aged 80; died, April 8, of carcinoma of the stomach.

Frederick Wallace Putnam, Binghamton, N. Y.; University of the City of New York Medical Department, 1880; aged 82; died, May 2.

William A. Marshall, Wharton, Ohio; Starling Medical College, Columbus, 1898; aged 73; died, May 8, in the Home and Hospital, Findlay.

John Randolph Comer, Hillsboro, Texas; University of Maryland School of Medicine, Baltimore, 1892; also a minister; died, April 27.

Jesse Wallace Powell, Millen, Ga.; Meharry Medical College, Nashville, Tenn., 1918; aged 48; died, May 18, of cerebral hemorrhage.

George T. Love ● Wenona, Ill.; Hospital College of Medicine, Louisville, Ky., 1897; aged 66; died, May 1, in St. Mary's Hospital, Streator.

H. D. Ford, Chicago; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1874; died in May of injuries received in a fall.

Joseph R. Burchell, Manchester, Ky.; University of Louisville Medical Department, 1877; aged 88; died, May 24, of lobar pneumonia.

Norbert Rieser, New York; Albert-Ludwigs-Universität Medizinische Fakultät, Freiburg, Baden, Germany, 1921; aged 43; died, May 3.

Albert Roy Bickstein, Philadelphia; Medico-Chirurgical College of Philadelphia, 1905; aged 54; died, April 27, in the Jeanes Hospital.

George Henry Calkins, Buffalo; University of Buffalo School of Medicine, 1893; aged 76; died, May 12, of carcinoma of the prostate.

Herbert Henry Thompson ● Minneapolis; Jefferson Medical College of Philadelphia, 1909; aged 55; died, May 22, in Fort Snelling.

Harry Albertus Brown ● Whitinsville, Mass.; University of Vermont College of Medicine, Burlington, 1895; aged 67; died, May 7.

John Collins Leever, Defiance, Ohio; Miami Medical College, Cincinnati, 1880; aged 84; died, May 13, of carcinoma of the stomach.

Harry Homer Dally, Chicago; Rush Medical College, Chicago, 1902; aged 60; died, May 20, in Kempton of cerebral hemorrhage.

William Ellsworth Barnes, Boston; Boston University School of Medicine, 1893; aged 77; died, May 5, of coronary thrombosis.

Locke Harwood Bugbee, Putney, Vt.; Dartmouth Medical School, Hanover, 1902; aged 65; died, May 24, of coronary occlusion.

Willis Bryant Moore, San Diego, Calif.; Halifax Medical College, Dalhousie, N. S., Canada, 1879; aged 83; died, April 13.

Frederick James Hosking, Hillsdale, Ont., Canada; University of Toronto Faculty of Medicine, 1934; aged 33; died, May 14.

William Jeter Quinn, Dallas, Texas; Barnes Medical College, St. Louis, 1896; aged 65; died, May 23, in the Baylor Hospital.

James Massie Gleason, Amonate, Va.; Medical College of Virginia, Richmond, 1932; aged 32; died, May 25, of heart disease.

Thomas C. Hainline, Seaton, Ill.; Keokuk (Iowa) Medical College, 1897; aged 81; died, May 19, of an injury received in a fall.

Willis Monroe Hunter, Van Wert, Ohio; Baltimore Medical College, 1892; aged 72; died, May 21, of cerebral hemorrhage.

James Clay Ross, Marion, Ind.; Louisville (Ky.) Medical College, 1906; aged 61; died, May 3, of cerebral sclerosis.

Joseph F. Barton, Jasper, Ala. (licensed in Alabama in 1903); aged 68; died, May 20, of cirrhosis of the liver.

Willard E. Gant, Hardin, Mo.; St. Louis Medical College, 1884; aged 79; died, May 4, of a cerebral hemorrhage.

James Wilson Edgar, Hamilton, Ont., Canada; University of Toronto Faculty of Medicine, 1891; died, May 7.

John Wylie Anderson, Denver; Hahnemann Medical College of Philadelphia, 1882; aged 81; died in May.

Joseph M. B. Johnson, Birmingham, Ala.; Miami Medical College, Cleveland, 1883; aged 81; died, April 29.

John Jerome Anderson ● Brooklyn; Long Island College Hospital, Brooklyn, 1911; aged 54; died, May 30.

Andrew Brown, Markdale, Ont., Canada; University of Toronto Faculty of Medicine, 1902; died, May 3.

Charles B. Brewster, Eustis, Fla.; Pulte Medical College, Cincinnati, 1904; aged 62; died, April 24.

Alfred Olaf Peterson ● Omaha; Omaha Medical College, 1899; aged 66; died, May 9, of leukemia.

Correspondence

SUBSIDIZED RESEARCH

To the Editor:—In Correspondence in THE JOURNAL July 15 Dr. J. A. Buchanan comments on the subsidized "researches" undertaken for the purpose of furnishing advertising propaganda.

Dr. Buchanan's letter echoes, I am sure, what many have felt but few, unfortunately, have bothered to express. As Dr. Buchanan says, "experience has demonstrated that too frequently the recommendations have been influenced by the subsidy."

It is indeed high time that the prostitution of the profession in this manner should be, as Dr. Buchanan suggests, recognized as a disgrace, declared unethical and suppressed. Certainly, if such "researches" and "clinical studies" are undertaken in good faith, there should be no reason to conceal the fact that they are subsidized or the amount of the subsidy and its source.

As it is, such practices are more malodorous than scientific, inspire neither respect for the "eminent authors" nor confidence in their observations, and tend, in the long run, to arouse grave doubts of the good faith of the sponsor broadcasting them ad nauseam.

R. A. KILDUFFE, M.D., Atlantic City, N. J.

RELIEF OF PAIN IN CHILDBIRTH

To the Editor:—Relative to the editorial "Relief of Pain in Childbirth" in THE JOURNAL June 24, may I remark that we introduced in the obstetric service of Johns Hopkins Hospital the rectal administration of sodium amytal in the fall of 1927. The late Dr. Whitridge Williams took particular interest in this new development and reported our observations in the sixth edition of his textbook of obstetrics, in 1931. Residents of various obstetric services in this country who visited our institution had the opportunity of watching patients under amytal analgesia. In an article in the September 1938 issue of the *American Journal of Obstetrics and Gynecology* on the intravenous administration of postpituitary extract (page 524) I remarked: "In 1928, the rectal administration of amytal was introduced. Our observations of rapid cervical dilatation, considerable alleviation of pain, amnesia, regularity of uterine contractions have been confirmed by several investigators. The evidence now at hand shows that the postpituitary oxytocic effect is not abolished in the parturient woman by amytal or nembutal twilight sleep."

J. I. HOFBAUER, M.D., Cincinnati.

FRACTURE OF THE SPINE COMPLICATING METRAZOL THERAPY

To the Editor:—An article published recently in THE JOURNAL (June 3, p. 2240) entitled "Fracture of the Spine Complicating Metrazol Therapy" by B. T. Bennett Jr. and C. P. Fitzpatrick made the statement that "the roentgenogram showed compressed fractures of the eleventh and twelfth dorsal vertebra. This was considered a rare and unfortunate occurrence, the first of its nature reported in the history of metrazol therapy" (p. 2241). On page 2243 it was stressed that "this preliminary report directs attention to a previously undescribed condition, compressed fracture of the vertebra resulting from metrazol convulsive therapy."

Historically, credit should be given to an article by Harry Stalker which appeared in the *Lancet*, Nov. 19, 1938, page 1172, in which "a double vertebral compression fracture from convulsive therapy" was reported. This paper was abstracted for the *Archives of Neurology and Psychiatry* by me, the substance of which is as follows: Following the second convulsion brought about by 1 cc. of triazol, a man aged 25 with paranoid schizophrenia complained of severe pain in the back and was unable to move. Examination revealed localized tenderness and a deformity over the sixth and seventh thoracic spines with no neurologic signs. X-ray examination revealed compression fracture of these two vertebrae. With the exception of dislocation of the jaws of patients, this was the only accident encountered in a series of fifty patients treated with convulsive therapy.

CHARLES M. KRINSKY, M.D., Boston.

BASAL METABOLISM TESTS

To the Editor:—A common method of connecting the patient to apparatus for a basal metabolism test is by means of a rubber mouthpiece. The nose is closed by means of a nose clip. With some patients this works very well but with many patients with large or irregularly shaped nostrils the clip has to be made extremely tight and set just so or a leak occurs.

The apparatus may provide a shiny metal mirror for testing for leaks, but after the nose clip is adjusted the patient may wrinkle the nasal muscles and change the position of the clip sufficiently to cause a leak to occur again.

This leak invariably causes a "high" reading. Also a tight nose clip gives the patient as much discomfort as any other part of the procedure, if not more.

The following simple addition to this procedure will prevent this leakage: Before the nose clip is fitted, the vestibules of the nose are filled with a firm, nonirritating ointment. Boric ointment is satisfactory, an amount the size of a pea being used in each vestibule, after which the nose clip is placed on the nose with but little tension. It is not necessary to bring the edges of the vestibule together. If the patient then wrinkles the nose or changes the position of the clip, the ointment will retain the seal. The excess ointment may be wiped off and the smooth appearance of the ointment will give visual evidence of the seal.

H. W. SEIGER, M.D., Ocean Park, Calif.

DETERMINATION OF PROTHROMBIN

To the Editor:—In this column there recently appeared a note by Dr. Armand J. Quick dealing with prothrombin tests as applied to the control of vitamin K therapy (June 17, p. 2552). One such test, advocated by our laboratory, consists simply of mixing thromboplastin (a simple saline extract of lung) with whole blood and observing the clotting time (Ziffren, S. E.; Owen, C. A.; Hoffman, G. R., and Smith, H. P.: *Proc. Soc. Exper. Biol. & Med.* **40**:595 [April] 1939). The clotting time is normally from twenty-five to thirty seconds but is typically prolonged when the prothrombin level is low. Dr. Quick objects to this test on the ground that clotting times cannot be measured accurately at the bedside. We have had no particular difficulty in this respect. A stop-watch is desirable, but even this is not essential, for an error of two seconds affects the result by less than 10 per cent.

The technic preferred by Dr. Quick is more complex, for in his test oxalated plasma is recalcified and then treated with thromboplastin. A centrifuge and water bath are needed. The amount of calcium added is arbitrary and the clotting mixtures are hypotonic. We have found that this affects the test.

In the article cited we have shown that both Quick's test and the bedside test are affected by factors other than the prothrombin level. However, careful analytic work has shown that in vitamin K deficiency a prothrombin deficit does exist and is the essential cause of the bleeding which occurs. Under these restricted circumstances either of these tests will give an accurate index of the tendency to bleed. The bedside test avoids many of the theoretical difficulties inherent in the technic of Quick, in addition to having the practical advantage of extreme simplicity. It thus seems to be the method of choice for control of vitamin K therapy in clinical work.

The question of priority for the bedside test is somewhat academic. The mixing of blood and thromboplastin is a very

old experiment, and of course neither Quick nor we can claim priority for that. All of his experiments with thromboplastin and whole blood were in cases presenting normal prothrombin levels. His belief that low prothrombin levels would be detected by such a test was an assumption for which he provided no data. Our own studies appear to be the first in which thromboplastin was actually used to test the blood of patients low in prothrombin.

H. P. Smith, M.D., Iowa City.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

VENETIAN BLINDS AND EYESTRAIN

To the Editor:—During the past few years so many cases of defective vision and eyestrain have been brought to my attention wherein the cause has been traced theoretically by me to Venetian blinds, that I am most curious to know whether there are any statistics or literature on this subject. The general symptoms seem to start with a "sort of wavering of the vision for a few moments before clear focus is achieved," and all complain of strain across the forehead, just at the level of the eyebrows, as though it was necessary to narrow the vision horizontally in order to see clearly. This of course was the basis of my theory of the Venetian blind factor. In every instance in which such symptoms have been expressed the patient was using Venetian blinds either in the home or in the office. I have questioned every one among my acquaintance using Venetian blinds, aside from those with a disorder of the eyes, and have received the same report from all, that Venetian blinds cause an optical illusion of wavering, until proper focus is adjusted, and after looking through them the retina retains the picture of the slats for some time and even occasionally when the vision is changed from distance to close or vice versa. This may prove interesting. M.D., California.

Answer.—The after-image produced by looking through Venetian blinds must be of the same basic value as that produced by looking through any other medium which obstructs all or part of the field of vision. After-images vary of course in intensity, but those produced through contrast between bright daylight (as seen between the slats of a Venetian blind) and the slats themselves must be of minor intensity, as after-images go, and retinal fatigue can scarcely result from such contrasting images. A more likely source of distress would be fatigue of the ciliary muscle in its attempt to adjust the curve of the lens to focus on any unusual object in the field of vision. But here also the stimulus would appear to be too weak to produce fatigue of a ciliary muscle which was otherwise meeting all demands made on it. The possibility of coincidence of a refractive error needing correction and the use of Venetian blinds is of course great.

Positive and negative after-images of windows were described by Peiresc in 1634, and the rather extensive subsequent bibliography can be found in Helmholtz. This whole question is dealt with rather fully (except that the phrase "Venetian blinds" was not then known) in Helmholtz's Physiological Optics, the first edition in 1866 and the third edition in 1909. This was translated by the Optical Society of America into English and published in three volumes in 1921. The material in question appears in the second volume, pages 172 to 299.

SODIUM THIOCYANATE IN HYPERTENSION

To the Editor:—Could you give me any information or cite references concerning the pharmacologic action and advisability of the use of sodium thiocyanate in hypertension? M.D., Michigan.

Answer.—The first recorded studies on the pharmacology of the thiocyanates were those of Pauli in 1903 (*München. med. Wchnschr.* **50**:153 [Jan. 27] 1903). Westphal (*Ztschr. f. klin. Med.* **101**:545, 1925) made the first extensive clinical investigations in 1925. Since then medical literature has contained a great many reports. The exact pharmacodynamics of the thiocyanates is not yet fully understood; it is presumed that they act directly on the arteriolar musculature in diminishing hypertonus. A complete bibliography is beyond the scope of this reply.

Sodium or potassium thiocyanate is an effective vasodilator, but the salts are toxic. The margin between toxic and clinically effective doses is close. Much of the literature deals with the therapeutic results obtained in series of cases of hypertensive arterial disease and the frequency with which toxic manifestations appear. The usual dose is from 0.3 to 1.0 Gm. a day in divided doses. The symptoms of poisoning have been previously discussed in this section of The Journal (Queries and Minor Notes, Feb. 24, 1934, p. 637). In 1936 Barker (The Journal, March 7, 1936, p. 762) instituted closer control of his patients on thiocyanate medication by frequent analyses of the thiocyanate content of the blood. By maintaining a blood concentration of from 6 to 12 mg. per hundred cubic centimeters of blood he was able to avoid precarious intoxications and yet obtain the maximum hypotensive activity of the drug. Individual susceptibility has an important part in the intoxications. In view of the risks of overdosage in cases in which renal elimination is impaired, thiocyanate should not be prescribed unless such control is included in the management. O'Hare and his co-workers (Massie, Edward; Ethridge, C. B., and O'Hare, J. P.: *New England J. Med.* **219**:736 [Nov. 10] 1938) have emphasized the urgent desirability of making the blood analyses at frequent intervals. This can be done with relative ease, since Griffith and Lindauer (*Am. Heart J.* **16**:710 [Dec.] 1937) introduced a micromethod for measuring the thiocyanate content of the blood in 1937. Although the analytic measures employed are by no means highly sensitive, they are sufficiently accurate for most clinical purposes.

ELECTRIC ARC WELDING AND IMPOTENCE

To the Editor:—Have you any information regarding impotence in males who are engaged in electric arc welding? A patient of mine, aged 34, is unable to have an erection; the condition has been present about six months and began shortly after he began doing arc welding. Complete physical examination, the Kahn reaction and examinations of blood and urine are negative. His diet and his domestic relations are above the average. There is no history of gonorrhea and there are no signs of prostatic disease. The testes are of normal size and are not tender. Secondary sex features are normal. This man has been using gasoline that contains tetra-ethyl lead to wash his hands and for other cleaning operations on machinery. Would this cause his trouble?

Philip V. Dreyer, M.D., Huntsville, Mo.

Answer.—At one time or another most occupations have been suspected of being a factor in sexual impotence. In a recent inquiry within the dry cleaning industry, the most frequent complaint against chlorinated hydrocarbons was that they caused impotence. When recently one manufacturer provided sodium chloride tablets for the prevention of sodium chloride fatigue, indignant protests were made by workers that the management was providing a sexual sedative. Such suspicions endlessly recur in industry, and on occasion a few have been dignified by medical publications. Lately apprehension has arisen lest working within the electrical field of the ultra high frequency short wave radio-casting equipment might cause impotence and sterility in both males and females. Since in this field of work it is possible that multiple electrical fields may be set up in body organs, these claims cannot be laid aside as preposterous. They are, however, unproved. With regard to electrical welding, Holstein in 1930 (*Zentralbl. f. Gewerbehyg.* **7**:286, 1930) claims that electrical welding is capable of harm to genital functions owing to structural damage to testicular tissues. Also welding has been associated with impotence in a Russian publication by Yakobson in 1935 (Effect of Electrical Welding, *Sovet. vrach. gaz.*, p. 1771, Nov. 30). Without denying the possibility, it may be pointed out that in arc welding the chief potential exposures are to ultraviolet rays, ozone, various oxides of nitrogen and heat. Not one of these exposures is known to be capable of producing sexual impotence as the sole manifestation. The fact that nitrogen compounds may be produced in arc welding may be the basis for the belief that sexual impotence is produced, since it is an age old tradition that some inorganic nitrogen compounds constitute sexual sedatives. Whenever any debilitating occupational disease arises such as lead or benzene poisoning, sexual capacity may be diminished or temporarily disappear. The same would be true in nonoccupational diseases such as typhoid or pneumonia. It may be definitely stated that impotence will not arise as the sole and exclusive manifestation of any occupational disease, with the possible exception of damage from roentgen rays.

It is well known that one action of lead and lead compounds, both in human beings and in the lower animals, is to damage sexual tissues and to promote sterility, abortions, miscarriages and the like. It is to be believed, however, that this will not arise in the absence of other and more characteristic features of lead poisoning. There exists scant evidence, if any, that

V 19

the nitrogen compounds produced in welding will exert any direct or primary action other than on the respiratory tract.

Functional impotence is distinctly related to the individual. The fundamental causative factors are emotional and psychologic. In the absence of demonstrable organic disease, patients with impotence, if needing any investigation and treatment whatever, usually prosper best when guided by psychiatrists.

DERMATITIS FROM PITCH

To the Editor:—A patient employed as a roofer has had his face exposed to the fumes of hot pitch. Petrolatum, ordinarily used as a prophylactic on the face, had been neglected. The face shows bullous parallel cracks of the epidermis of the exposed parts except for the nose, which shows only redness and edema. Since this is the first case I have seen, I should like to know more about pitch fume dermatitis, which I presume it to be.

Hubert C. Miller, M.D., Racine, Wis.

ANSWER.—Dermatitis and melanosis are not of unusual occurrence among workers exposed to the fumes or dust of coal tar distillates, especially coal tar pitch. Sunburn and melanosis are caused by the photosensitizing effect of coal tar derivatives on the skin. Some workers exposed to these substances sunburn more easily and more severely than normal persons, while in others melanosis develops. Sensitivity to some of the constituents of coal tar would also cause an urticarial dermatitis of the exposed parts.

Occupational keratoses, papillomas and epitheliomas may also be caused by long exposure to coal tar products.

Distillers of coal tar, roofers, road makers, briquet makers, fiber conduit makers and those engaged in preserving wood with creosote oil are some of the workers exposed to these skin hazards.

This subject is discussed more fully by Harry R. Foerster and Louis Schwartz (Occupational Melanosis from Pitch, *Arch. Dermat. & Syph.* **30**:955-968 [June] 1939; Industrial Dermatitis and Melanosis Due to Photosensitization, *ibid.* **30**:55-68 [Jan.] 1939).

DECREASED INSULIN REQUIREMENT IN THE DIABETIC

To the Editor:—Is it true that a few diabetic patients, even though they are considered to have the disease in a severe form, are either cured of the disease later in life or can cut down on their insulin a great deal? This question is asked by the husband of one of my patients who has diabetes in a severe form. I could not answer him as to whether or not it was true or false. The patient developed diabetes in 1924 at the age of 12 years and has been taking insulin in large amounts ever since. In January 1938 she went into coma and after she was brought out of it she was put on a regimen of 15 units of ordinary insulin before breakfast and 65 units of protamine zinc insulin at 11 o'clock in the morning. She also was on a diet and this she adhered to faithfully. She got along fine on this amount of insulin until October 1938, when she developed an insulin shock during the night. Dextrose was given intravenously and she recovered. I then had her test her urine at bedtime and had her cut her protamine zinc insulin down 2 units at a time until she was showing a trace of sugar at bedtime. Since that time she has cut her protamine insulin down to 43 units at 11 a. m. but the other night she had a mild insulin reaction. She is also at times having mild reactions in the morning about four hours after taking the regular insulin. I have given instructions to cut that down 2 units at a time and to test the urine four hours later. The patient has been on the same diet that she started in January 1938 and weighs about the same as she did at that time. She has not been working any harder than she did a year ago either. However, she was married shortly before she began to have trouble with her insulin dosage. She is not pregnant. An answer to this inquiry would be greatly appreciated by the patient and me if it is possible for you to do so.

M.D., Iowa.

ANSWER.—Few physicians wish to risk their reputations by stating that persons with diabetes are cured because, although patients advancing in age with the duration of their diabetes may show little or no glycosuria and no hyperglycemia under ordinary conditions, yet in the presence of infection the diabetes again becomes active. It is true that some patients are enabled to reduce the quantity of insulin. This is more apt to occur in the young during the years following adolescence and among older persons. It is a common observation that patients entering a hospital with an infection may require large doses of insulin but in the course of a few weeks under the influence of dietary treatment or subsidence of infection or both may require little or no insulin even with a liberal diet.

As for this patient who developed diabetes in 1924 at the age of 12 years and has depended on 80 units of insulin (15 regular and 65 protamine), it is not surprising that she should have improved and have had an insulin reaction. For such cases it usually is wise regularly to give carbohydrate not only in the latter part of the forenoon and afternoon, but on retiring a little protein and fat in addition, such as cottage cheese or a few nuts to prolong the absorption of the carbohydrate. One should give the luncheons always and not alone when the urine is sugar free and plan the insulin accordingly. Apparently marriage agrees with the patient. Life may be more uniform, the diet may be more appropriately carried out and slight changes in times of meals and exercise may have contributed to the good results, even apart from happiness.

It would be worth while to try the effect of giving the two types of insulin by separate injection in the morning before breakfast with no more insulin during the rest of the day. Then two tests of urine become important in the subsequent regulation of dosage: (1) the test of a specimen before breakfast (not the overnight specimen), which indicates the effect of the protamine zinc insulin given on the previous morning, and (2) the test of a specimen voided just before the noon meal, which indicates the effect of the regular insulin taken on that day. Changes in either or both types of insulin may be made 2 or 4 units at a time, two or three days being allowed between changes.

ALUMINUM PAINT AND THE EYES

To the Editor:—What effect will the spraying of aluminum paint have on the eyes and, if any, what is the prophylaxis and treatment? I understand that this paint is made by mixing aluminum with a cheap grade of varnish. Please give me what information you have on this subject.

M. E. Rust, M.D., Powhatan, Ohio.

ANSWER.—Powdered metallic aluminum possesses no chemical properties detrimental to the eyes. Mechanical injury might arise, just as from any other solid ingredient of paints. Liquid vehicles for aluminum paint may be more damaging to the eyes. In earlier days, aluminum powder was suspended in lacquer types of menstruums with amyl acetate (banana oil) as the commonest ingredient. At the present time, some aluminum paints are still so made. Vapors from these lacquers are well known causes of minor degrees of conjunctivitis. Better grade aluminum paints utilize different vehicles, depending on the purposes for which the coating is supplied. For automobile motors and similar metal equipment an ester gum varnish now enjoys wide use. For outdoor purposes the vehicle represents a synthetic resin varnish.

Numerous different solvents may enter these varnishes, including toluene, naphthas, turpentines and at times alcohols. Any one of these divers substances, in addition to possible effects elsewhere, may cause conjunctivitis on direct contact with the eyes and many may induce mild conjunctivitis on contact with their vapors. However, the low order of irritation from the vapors of aluminum paint ordinarily calls for no special prophylactic measures. When the work is continuous, spraying should be carried out only in booths. Either water or air carriage type of booths properly constructed and operated are satisfactory. Occasional jobs not requiring booths should never be performed in small closed-off spaces, such as the interior of a tank or a small room. Since the lacquer types of aluminum paints are more injurious than others, this variety should be avoided as a prophylactic measure. Positive pressure hoods with open faces are quite effective in warding off the deleterious action of this class of paint.

INSULIN REACTIONS AFTER BEE STINGS

To the Editor:—A diabetic patient is taking 51 units of insulin daily. During the last year his duties have included the care of ten hives of bees. It is his impression that his general condition has been much improved since taking over this new occupation. He has observed on numerous occasions that multiple bee stings are followed by an insulin reaction. In one instance, when a hive was upset and he was stung twenty-five or fifty times in one day he omitted 10 units of insulin from his regular dose, in spite of which he suffered a series of insulin shocks. Although the story sounds plausible when told by the patient, I wonder whether it has any scientific basis. Would you kindly let me know if there have been any previous observations of this sort?

Paul Geary, M.D., Plainfield, N. J.

ANSWER.—No information is available as to the possible effect of multiple bee stings on the blood sugar. Certainly one would demand that accurate data be supplied as regards the level of blood sugar before and after contact.

Is it not possible that the patient in question is more active physically at his new occupation than he was before and, because of this additional physical exertion, that he has obtained the customary beneficial effects of exercise as regards the control of his diabetes? Is it not possible also that, on the day on which he suffered from twenty-five to fifty bee stings, he was even more active than usual and that his bodily feelings were such that less food was consumed?

POSSIBLE INTERMITTENT CLAUDICATION

To the Editor:—A man aged 58, a bachelor of Italian birth, came to this country from the Italian Alps region in 1911. His chief complaints are cramps, pain and weakness in the muscles of the calves of the legs on walking short distances (one or two city blocks at times, whereas at other times he is able to walk considerably further without trouble). On these occasions he says that his back also becomes weak and tired but not sore. On mild exertion, such as shoveling snow, he also gets the symptoms. When he writes a few lines, the muscles of his hands also become weak and tired and he may have difficulty in adducting the fifth finger of his left hand. On arising in the morning he has difficulty in buttoning his clothes while dressing, owing to weakness and awkwardness in the use of fingers, but this improves in a few hours. He states that he has had these symptoms all his life as long as he can remember. He says that his older brother had the same condition. This brother served in the World War but died shortly after being mustered out of the Italian army. The patient himself remembers that at the age of 20, while in service in the Italian army, he could never walk or march long distances. He always had to drop out of line and quit with weakness because he just couldn't go any further, while his colleagues all kept marching along. He saw brief service in the World War at Camp Grant, Rockford, Ill., but was shortly discharged because of this persistent inability to walk longer distances. He has never been able to work hard because of this condition and therefore was never able to earn enough to marry and support a family. He eles out a meager existence running an automobile parking lot. He has observed on occasions that if he drinks a glass of beer it produces a remarkable change in his powers of endurance. On such occasions he can walk for many blocks without any evidence of fatigue, and though he doesn't like alcohol, he does drink a little occasionally whenever it is necessary for him to walk far. Formerly he smoked five or six corncob pipefuls of tobacco a day and one or two cigars but he has not done this in recent years. Otherwise the history and the physical and neurologic examinations are negative. The blood count is normal and urinalysis and the Wassermann reaction of the blood are negative. The condition looks like intermittent claudication, but all the peripheral arteries are patent and pulsate well, including the radials, tibialis posterior and dorsalis pedis arteries on both sides. There is also no muscular atrophy to suggest primary muscular atrophy or dystrophy. He has been examined by many different physicians both in this country and in Italy over a period of many years, and no one has ever been able to make a diagnosis. The condition sounds to me like a congenital vascular (arterial) insufficiency with improvement after vasodilatation by alcohol. Could you suggest to me any other diagnosis or give me some ideas regarding treatment?

M.D., Milwaukee.

ANSWER.—The subjective complaints are compatible with a diagnosis of intermittent claudication, in all probability based on a congenital vascular abnormality of the peripheral blood vessel system. The fact that there is good pulsation in the peripheral vessels does not militate against a diagnosis of peripheral vascular disease. His weakness and awkwardness in the use of his fingers on arising may be due to a peculiar posture during sleep, causing pressure on an already abnormal vessel. It is not stated whether any of the tests have been done for patency of the vessels and for degree of possible vascular dilatation. These are the following: intradermal injection of histamine to determine the extent of flare formation; intravenous injection of typhoid vaccine to determine the degree of rise in temperature of the surface skin of the extremity; color changes in the dependent and elevated positions, and finally peripheral nerve block with cocaine. The latter differentiates organic from spastic occlusion. If significant changes are found one may inject tissue extract (vasodilator) two or three times a week or give some vasodilator drug by mouth. It is possible, if no abnormal changes are found with these tests, that the patient has myotonia congenita. If that is so, the giving of quinine hydrochloride 0.3 Gm. (5 grains) three or four times a day may effect improvement.

HORMONES IN DEAFNESS

To the Editor:—Kindly give me information or references concerning the treatment of deafness with hormones or glandular products. What is the opinion concerning their value?

M.D., Kentucky.

ANSWER.—Hormones and glandular products have been used in the treatment of deafness by various investigators and by several routes of administration.

Mortimer, Wright, Thomson and Collip of Canada have reported recently on the intranasal administration of estrogenic hormones in constitutional deafness (*Canad. M. A. J.* **40**:17 [Jan.] 1939). This work was suggested by a study of cranial dysplasia, its presence in cases of constitutional deafness and a similarity in examinations of persons suffering from atrophic rhinitis. The deafness was of both the conduction and the perception type, and the audiometric records purport to show a statistically significant amelioration in the hearing level of the treated group. Despite this, the evidence appears unconvincing, especially if there was true otosclerosis or persons suffering from nerve deafness in the group studied. It seems unlikely that such a high percentage of cases presenting atrophic rhinitis should also present these specific hearing difficulties, for such an association has not been noted by others. On the other hand, it is true that if the deafness in these cases was on the basis of a chronic catarrhal otitis media secondary to an atrophic rhinopharyngitis, treatment with estrogenic substances intranasally, as has been efficacious in atrophic rhinitis, would similarly be expected to help the hearing defect.

The treatment of otosclerosis by the intratympanic injection of thyroxine as first advocated by Gray and endorsed by Goldstein in this country must be also considered. It would seem that in some cases favorable results have been obtained. The method has not been widely accepted or adopted to date, however.

References:

Blaisdell, I. H.: Use of Estrogenic Substances in Atrophic Rhinitis, *Laryngoscope* **48**:699 (Oct.) 1938.
Goldstein, M. A.: *Tr. Am. Laryng., Rhin. & Otol. Soc.* **44**:118, 1938.

FORMOL-GEL TEST FOR RHEUMATIC FEVER

To the Editor:—Will you please describe the technic of the formol-gel test of Gutt and Papocostas?

M.D., New York.

ANSWER.—The formol-gel test may be performed as follows: To 1 cc. of serum in a test tube (8 mm. bore is a convenient size) add 2 drops of from 30 to 40 per cent formaldehyde, mix and allow to stand at room temperature. Normal control serums show no change in viscosity or transparency in twenty-four hours. With pathologic serums gelation, with or without opacity, may occur during this time. Following the suggestion of Gutman and Wise (*Proc. Soc. Exper. Biol. & Med.* **38**:124 [Oct.] 1936), the results of the tests may be expressed as follows:

Gelation	Opacity
— = no increase in viscosity	— = no change
± = questionable increase in viscosity	± = questionable slight opalescence
+ = increased viscosity	+ = opalescent
++ = very viscous flow	++ = translucent
+++ = semisolid	+++ = semiopaque
++++ = solid	++++ = opaque

FIRST BREAST MILK

To the Editor:—Could you give me any information concerning the advisability or inadvisability of discarding the first breast milk obtained under sterile precautions by the use of an electric breast pump in a hospital following the birth of a child? Let it be taken for granted that the indication of the use of the electric breast pump is proper and advisable in the particular case and the patient either a primipara or a multipara. Many hospitals discard this milk.

M.D., Wisconsin.

ANSWER.—There is seldom any reason to discard the first breast milk obtained with a breast pump. Certainly this should not be done as a routine. The only time it is justifiable to discard the first or subsequent few specimens of milk obtained with a breast pump is when the mother is seriously ill or has been given large doses of drugs which are eliminated through the breast milk and which may have a harmful effect on the baby.

BIBLICAL REFERENCES TO MENSTRUATION

To the Editor:—Would you be so kind as to furnish me with information whereby I may locate passages in the Bible that refer to the function of menstruation?

Samuel C. Goyne, M.D., Worcester, Mass.

ANSWER.—The following are the main places where menstruation is mentioned in the Bible: Genesis 31:35, 18:11, Leviticus 15:19-33, 18:19, 20:18. Ezekiel 18:6, 22:10. The passages in Leviticus are concerned with ritual uncleanliness during menstruation and the prohibition of intercourse. Genesis 18:11 shows that the relation between the menopause and childbearing was known. For a general discussion of menstruation in Biblical and Talmudic literature see: Preuss, Julius: Biblisch-talmudische Medizin, ed. 3, Berlin, S. Karger, 1923, page 138, and Brim, C. J.: Medicine in the Bible, New York, Froben Press, 1936, page 188.

GONADOTROPIC SUBSTANCE AND TUBERCULOSIS

To the Editor:—Please advise me whether the injection of gonadotropic substance from the urine of pregnancy for the treatment of oligospermia is contraindicated in a patient aged 28 with incipient tuberculosis.

M.D., Philippine Islands.

ANSWER.—The use of gonadotropic substance from the urine of pregnancy is not contraindicated in a patient suffering from incipient tuberculosis.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in THE JOURNAL, August 5, page 531.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Medical centers having five or more candidates desiring to take the examination, Sept. 11-13. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th Street, Philadelphia.

SPECIAL BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: An Affiliate of the American Board of Surgery. *Written.* Various places throughout the United States, Sept. 9. *Oral.* Part II. Philadelphia, Oct. 14-15. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written.* Various large cities in the country, Oct. 9. *Applications must be received by the Secretary by Sept. 1. Oral.* Philadelphia, Nov. 3-4. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Various sections of the United States, Oct. 16 and Feb. 19. Formal application must be received before Aug. 20 for the Oct. examination and on or before Jan. 1 for the Feb. examination. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written examination and review of case histories (Part I) for Group B candidates* will be held in various cities of the United States and Canada, Jan. 6. *Applications for admission to Group B, Part I, examinations must be on file not later than Oct. 1. General oral and pathological examinations (Part II) for all candidates (Groups A and B)* will be conducted in Atlantic City, N. J., June 8-11. *Applications for admission to Group A, Part II examinations must be on file not later than March 15.* Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* March 9. Formal application must be received before January 1. *Oral.* Chicago, Oct. 7 and New York, June 10. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Boston, January. *Applications must be filed on or before Nov. 1.* Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: Chicago, Oct. 6-7. Sec., Dr. W. P. Wherry, 1508 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PATHOLOGY: Memphis, Nov. 22-23. Sec., Dr. F. W. Hartman, Henry Ford Hospital, Detroit.

AMERICAN BOARD OF PEDIATRICS: New York, April 30 and May 1. Kansas City, Mo., preceding the Region III meeting of the American Academy of Pediatrics. Seattle, preceding the Region IV meeting of the American Academy of Pediatrics. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, December. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: Atlanta, Ga., Dec. 9-11. Sec., Dr. Byrl R. Kirklin, 102-110 Second Avenue S.W., Rochester, Minnesota.

AMERICAN BOARD OF SURGERY: *Part I (Written).* Simultaneously in various centers throughout the United States, Oct. 9. *Applications must be received by the Secretary not later than Aug. 15.* Sec., Dr. J. Stewart Rodman, 225 S. 15th St., Philadelphia.

AMERICAN BOARD OF UROLOGY: Chicago, Feb. 9-11. (The only examination session to be held in 1940.) *Case reports must be submitted not later than November 9.* Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

Alabama June Examination

Dr. J. N. Baker, secretary, Alabama State Board of Medical Examiners, reports the written examination held at Montgomery, June 20-22, 1939. The examination covered ten subjects and included 100 questions. An average of 75 per cent was required to pass. Thirteen candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists		(1938)	80.7
Louisiana State University Medical Center		(1937)	89.9
Tulane University of Louisiana School of Medicine		(1939)	87.6,* 88.5,* 89.7,* 91.9*
Johns Hopkins University School of Medicine		(1939)	88.7*
Long Island College of Medicine		(1939)	85.8*
University of Tennessee College of Medicine		(1937)	80.3
Vanderbilt University School of Medicine		(1931) (1939)	82.8, 88.3*
Queen's University Faculty of Medicine		(1936)	93.8
McGill University Faculty of Medicine		(1936)	87.6

* License withheld pending completion of internship.

Montana April Report

Dr. S. A. Cooney, secretary, Montana State Board of Medical Examiners, reports the written examination held at Helena, April 4-5, 1939. The examination covered ten subjects. An average of 75 per cent was required to pass. Four candidates were examined, all of whom passed. Seven physicians were licensed by reciprocity and one physician was licensed by endorsement at the meeting held April 3. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Harvard Medical School		(1934)	86.6
University of Minnesota Medical School		(1939)	84.5
University of Oklahoma School of Medicine		(1938)	75.3
McGill University Faculty of Medicine		(1938)	79.1

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
College of Medical Evangelists		(1935)	California
Rush Medical College		(1937)	Iowa, Utah
University of Kansas School of Medicine		(1907)	Kansas
Harvard Medical School		(1926)	Rhode Island
Ohio State University College of Medicine		(1935)	Ohio
Baylor University College of Medicine		(1933)	Texas

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
St. Louis University School of Medicine		(1936)	N. B. M. Ex.

Book Notices

Silicosis and Lead Poisoning Among Pottery Workers. By Robert R. Flinn, Passed Assistant Surgeon, United States Public Health Service, et al. From the Division of Industrial Hygiene, National Institute of Health. Prepared by direction of the Surgeon General. United States Treasury Department, Public Health Service. Public Health Bulletin No. 244. Paper. Price, 30 cents. Pp. 178, with 78 illustrations. Washington, D. C.: Supt. of Doc., Government Printing Office, 1939.

This bulletin records the results of a resurvey of the most prominent physical defects encountered among workers in pottery factories originally observed in 1919. The value of reports of this kind is exemplified in the degree of control which has been established in the interim over exposure to lead. Once a major hazard in the pottery industry and still a potential source of trouble, the problem is being solved by engineering methods and by substitution of relatively nontoxic glazes for those formerly containing soluble lead compounds. A good share of the medical and engineering studies refer to silicosis. The criteria for establishing a diagnosis are emphasized both clinically and radiologically. Valuable verifying data are provided by means of illustrative x-ray films and case histories, two necropsy protocols and reports on peritoneal response to injected dust samples in guinea pigs according to the method of Miller and Sayers. Several interesting three dimensional charts have been developed regarding positive chest conditions in relation to length of exposure and concentration of dust. One infers that concentrations of dust can be held below 4 million particles per cubic foot and if so reduction in the incidence of silicosis will parallel the past records regarding lead poisoning. The incidence of tuberculosis has fallen off about in the same proportion as the industrial population in general. In this study active cases were discovered but could not be verified by sputum examination. The appended bibliography appears to be well chosen and the makeup of the bulletin is aided by a good index.

Iodine Metabolism and Thyroid Function. By A. W. Elmer, M.D., Institute of General and Experimental Pathology, John Casimir University, Lwów (Poland). Cloth. Price, $10. Pp. 605, with 23 illustrations. New York & London: Oxford University Press, 1938.

This book is material proof of the stupendous growth of the literature since 1895, when Baumann discovered iodine as a normal element of the thyroid. The contents are thoughtfully arranged in four chapters: (1) historical review, (2) methods of iodine determination, (3) physiology of iodine metabolism and (4) pathology of iodine metabolism.

The historical review is on the whole excellent but is open to the criticism of omission and unconscious distortion inherent in such efforts. One may reasonably doubt that Rabourdin's method as used by Chatin was capable of detecting 0.1 microgram of iodine or that Chatin's work, though of the greatest importance in retrospect, contemporaneously influenced the development of our knowledge of the biologic importance of iodine. The chapter on methods of iodine determination gives a complete and critical summary of the evolution of these methods. Sufficient detail is given to permit one to carry out the procedures for the examination of inorganic and organic substances. The sources of errors and dangers are well emphasized. In the chapter on the physiology of iodine metabolism one notes the absence of important names such as those of Murray, Howitz and Magnus-Levy, who through their clinical and physiologic studies greatly stimulated interest in thyroid chemistry. In some instances the wrong authors are given credit for observations. This must happen occasionally when great numbers of contributions are being summarized but should

not occur so frequently as in this book. For example, Holst (1928) is given credit for the thyroxine oversaturation theory of postoperative crises in exophthalmic goiter. In all essentials this was an old theory in 1905 and was reasonably discredited by 1910. The chapter on the pathology of iodine metabolism reviews the work on hypothyrosis and hyperthyrosis. It is doubtful whether much knowledge of the pathogenesis of hypothyrosis has been or will be gained from the study of iodine metabolism alone. In other words, iodine studies have about the same value as morphologic studies.

This book will be a valuable addition to any reference library because it brings together most of the laboratory and experimental literature dealing with the biologic importance of iodine. A complete table of contents makes reference to any particular topic easy, and sixty pages of carefully checked, complete bibliographic references is an item of major importance to any student.

The Control of the Circulation of the Blood. By R. J. S. McDowall, M.D., D.Sc., Professor of Physiology, University of London. King's College. With the assistance of G. E. Malcomson, M.D., Lt.-Col. I. M. S., and I. McWhan. Cloth. Price, $12.50. Pp. 619, with 38 illustrations. New York, Toronto & London: Longmans, Green & Co., 1938.

This is the most complete review of the literature on the physiology of the circulation yet available, encompassing as it does about 6,000 items in the bibliography. The senior author has long been recognized as an authority in this field; consequently one is not disappointed to find that, in addition to reviewing literature, he has given a scholarly analysis of the evidence bearing on many of the salient problems. Despite the great mass of material included, if one bears in mind the title there need be no surprise on finding that many phases of circulatory physiology are not discussed in detail. Evidently the aim was to confine the work to those factors which control circulation and there is consistent adherence to the plan. One could wish for a somewhat more systematic arrangement of material and a more detailed index. Also there is frequent reference to certain authors without any hint as to the nature of their work or to its place in the general alinement of evidence.

The illustrations are well suited to bring out pertinent points, but it would have been desirable to have many others graphically presented in view of the high degree of concentration of the textual evidence. There is not much direct reference to clinical applications per se, but the lucid exposition leaves no serious gap to be bridged by the clinician. This book presents a wealth of source material and, despite the defects, is a praiseworthy addition to the literature, especially for the busy physician who needs a condensed source of authority.

Health at Fifty. Edited by William H. Robey. Cloth. Price, $3. Pp. 299, with illustrations. Cambridge, Massachusetts: Harvard University Press; London: Oxford University Press, 1939.

The title fails to do justice to this excellent book, because it is too narrow. While the greatest emphasis is placed on health in the middle decades, the book is packed with information useful at any adult age. It is a compilation of chapters based on public lectures given by the faculty of the Harvard Medical School, a series of lectures which was inaugurated in 1907 and has been interrupted for only one year, 1919. There are eleven chapters dealing in turn with heart disease, blood pressure, weight control, cancer, rheumatism, the menopause, the eyes, vitamins, glands, the family medicine cabinet and mental health, plus a summarizing chapter by the editor. The material is well authenticated, well selected and well arranged. Unlike many compilations of lecture material in which each chapter is contributed by a different author, this book is not discursive and repetitious, which means of course that it comprises a good job of editing and correlating as well as a basis of fundamentally sound material. One wonders why consideration of the ears and hearing was not included, since this is a vital problem in the middle decades and beyond, as are pneumonia, bronchitis and the related infections of the respiratory tract, which also are omitted or treated incidentally to other subjects. Nephritis and diabetes receive only incidental attention, the latter in connection with glands and the former with blood pressure. The style is surprisingly constant in view of the fact that so many authors have contributed, but this is another indication of careful editing. The language is probably simple enough for lay readers with a good education and a willingness to refer to a dictionary once in a while, but there are a number of passages which might better have been simplified and made less technical for the so-called average reader. The best chapter in the book from the point of view of presentation and general usefulness to the lay reader is the one dealing with self medication and the family catch-all known by courtesy as the medicine chest. The book as a whole will certainly repay a careful reading. As a reference book it would have been improved by the addition of an index.

Evaluation of the Industrial Hygiene Problems of New Hampshire. By Frederick J. Vintinner, B.S., Industrial Hygienist. State of New Hampshire Board of Health. Division of Chemistry and Sanitation. Charles D. Howard, M.D., Director. Paper. Pp. 133, with 5 illustrations. Concord, New Hampshire, 1938.

This survey, which will be of greatest interest to physicians in New Hampshire, typifies the analysis of industrial hazards and present methods of control conducted recently by bureaus of industrial hygiene in a number of state health departments under the general guidance and stimulation of the United States Public Health Service. Sixty tables and the accompanying text present the character and extent of harmful exposures encountered by workmen in the area, including the availability of medical and nursing services, hospitalization, plant dispensaries, first aid arrangements and safety provisions in general. A series of recommendations is attached, sound and laudable for the most part but in which little mention is made of the possibilities for useful cooperation with organized medicine in the state or with individual industrial practitioners. This occurs in spite of a plea for better reporting of occupational diseases unattainable without considerable assistance from all types of physicians. Nevertheless the survey is useful not only as a catalogue of existing hazards but as a point of reference by which subsequent progress can be measured. It should be available to all physicians in the state in its complete form.

Report on Radium Beam Therapy Research 1934-1937. By Constance A. P. Wood, L. G. Grimmett, T. A. Green and others. Under the direction of the Governing Body of Radium Beam Therapy Research. Medical Research Council, Special Report Series, No. 231. Paper. Price, $1.50; 6s. Pp. 17, with 36 illustrations including 22 plates. New York: British Library of Information; London: His Majesty's Stationery Office, 1938.

This report records the result of four years' research into the treatment of cancer by means of the rays from a large mass of radium situated at a distance from the patient, as contrasted with the more usual type of radium therapy, in which much smaller amounts, properly contained, are inserted by surgical operation directly into the tissues or applied close to the skin. The former method, first developed in France, Belgium, the United States and, more extensively, Sweden, has been referred to as "radium beam therapy" or "teleradium therapy."

In the work represented by this publication, treatment was restricted to cancer of the mouth, tongue, pharynx and larynx, relatively accessible to radium therapy. By reason of the superficial sites of the growths, the local effects of the radiation could be readily observed. The results compared favorably with those to be expected from surgical intervention and were obtained without any mutilation of the patients. However, it is necessary to mention that the patient with cancer undergoing radium beam therapy cannot expect to escape a period of some discomfort during and immediately after the treatment, because of the effect of the radiation on the mucous membrane and the skin. This unpleasant reaction is characterized by difficulty in swallowing, loss of taste and dryness of the mouth, all of which disappear gradually after completion of the treatment. In patients whose lesions are still operable the treatment has given encouraging results, comparing favorably with those to be expected from operation. Of those with advanced or inoperable cancer, a few can be rendered free from disease and the remainder afforded a fairly satisfactory degree of palliation.

One interesting fact demonstrated in the preliminary studies of this research committee is that the unit roentgen (r) is applicable to radium as well as to x-ray therapy, provided certain precautions are taken, and the roentgen is now established as the international unit for both radium and x-ray therapy. This is a valuable bit of knowledge, for it will permit interesting and informative comparisons with parallel clinical investigations in x-ray therapy.

In a brief review it is impossible to present even a short abstract of the valuable methods devised, instruments invented and special technical maneuvers perfected. The latter half of the book is filled with illustrations, many of them in color, showing the progress of the disease in various lesions of the head, neck and jaw in various stages of treatment.

Dermatitis and Coexisting Fungous Infections Among Plate Printers. By Paul A. Neal, Passed Assistant Surgeon, and C. W. Emmons, Senior Mycologist. From the Division of Industrial Hygiene and the Division of Infectious Diseases, National Institute of Health. Prepared by direction of the Surgeon General. U. S. Treasury Department, Public Health Service. Public Health Bulletin No. 246. Paper. Price, 15 cents. Pp. 55, with 8 illustrations. Washington, D. C.: Supt. of Doc., Government Printing Office, 1939.

This report represents a careful study of the incidence of dermatitis in a group of plate printers exposed to a variety of mycotic, bacterial, mechanical and chemical skin irritants, the latter including colored inks and certain solvents used for cleaning plates. Through application of the criteria of Sulzberger it was determined that the dermatitis was industrial in origin although no single cause could be universally assigned. The authors recommend thorough physical examinations periodically of all employees, with routine patch testing for applicants. Past methods of hand cleansing are particularly criticized and suitable emphasis is placed on the need for cooperation by the employees in order that proper personal hygiene may contribute to the reduction of cutaneous irritation.

Röntgendiagnostik des Chirurgen. Von Professor Dr. Otto Kingreen, Leiter der chirurgischen Abteilung des städtischen Krankenhauses Lüdenscheid. Paper. Price, 30 marks. Pp. 324, with 527 illustrations. Leipzig: Johann Ambrosius Barth, 1939.

This edition presents the roentgenologic diagnosis of surgical conditions completely and in an easily readable form. The first chapter begins with an introduction to x-ray technic and familiarizes the surgeon with the properties of x-rays and the equipment of a diagnostic department. A brief description of the kymographic, tomographic and densographic methods follows. The last-mentioned method is a graphic presentation of the distribution of various densities of shadows in the form of curves and employs a photoelectric cell connected with a registering galvanometer. The second chapter treats of the localization of foreign bodies and offers a description of the calcifications and ossifications seen in roentgenograms; the third, with fractures and pathologic processes of bones and articulations; the fourth, with the examination of lesions of the internal organs of interest to surgeons, e. g. empyema of the chest, pulmonary tumors, diaphragmatic hernia, ulcers and tumors of the digestive tract, and pyonephrosis, and the fifth, with an explanation of special methods of examination such as arteriography, venography, contrast filling of articulations, hepatography, lienography and pneumoperitoneum.

The treatise is a thorough, comprehensive, well arranged and competent book. It has been written to meet the needs of the general surgeon and therefore avoids any subjects of a purely theoretical character. The features of conciseness and clearness of expression are prominent. From the typographic point of view the book is excellent, having been printed in an easy to read type and profusely illustrated with reproductions of roentgenograms. In spite of the small size of the illustrations, the details have not been lost. As a well trained surgeon should be able to read roentgenograms without depending entirely on the diagnosis of the roentgenologist, this unusually helpful book will make a place for itself in the medical world.

Der Operationskurs des Hals-, Nasen- und Ohrenarztes. Von Prof. Dr. H. Beyer und Prof. Dr. A. Seiffert. II: Die Operationen an Nase, Mund und Hals. Von Prof. Dr. A. Seiffert. Second edition. Paper. Price, 24.50 marks. Pp. 266, with 351 illustrations. Leipzig: Curt Kabitzsch, 1939.

For its size, this is a valuable book. There are numerous illustrations, including photographs of instruments, surgical conditions and anatomic details which make it exceedingly useful for the beginning specialist and for the postgraduate student. The text although brief is authoritative. For one interested in the point of view of the German school in the field of diseases of the nose and throat, the author presents a reliable treatise. However, because it varies so little from the first edition it should be called a reprint and not a second edition.

The Microscopical Study of Drugs. By Lilian A. Kay, B.Pharm., Ph.C., Lecturer in Pharmacognosy, Leicester College of Technology, Leicester. Fabrikoid. Price, $4. Pp. 228, with illustrations. Baltimore: William Wood & Company, 1939.

Pharmacognosy as a separate branch of pharmacy has lost ground in schools of pharmacy during the last twenty-five years. Rarely is a pharmaceutic chemist nowadays called on to identify botanic drugs. This task is left to the expert possessing the necessary technical and practical experience. To demonstrate, however, to the pharmacy student the methods used in the microscopic study of drugs the author has selected a number of well chosen examples in the laboratory outline. In this way the student interested in pharmacognosy becomes acquainted with practical problems of the pharmacognosist. The text is clear and well suited for self study, but one might have wished for the inclusion of a list of larger reference compendiums to stimulate the more industrious student during his laboratory work.

Spring Floods and Tornadoes, 1936: Official Report of Relief Operations. ARC 979. Paper. Pp. 173, with illustrations. Washington, D. C.: American National Red Cross, 1938.

This official report of relief operations during the spring floods and tornadoes in 1936 is an attractive publication, well illustrated with maps, diagrams, photographs and charts, all dealt with in the modern, pictorial, statistical manner. There is a chronological report of developments presented as a typical picture of disaster situations and necessary relief. The manner in which relief was mobilized from all available sources is graphically described. Considerable space is given to rehabilitation of the physical damage and of the social damage. There is a chapter on medical problems too brief to be adequate, especially in view of the space given to other phases of disaster relief. There are extensive statistical reports in a series of appendixes. There is an adequate index. Though a paper binding is used, the printing and makeup of the book are exceedingly attractive, owing to the effective handling of illustrative matter and the large clear type and numerous subject headings.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Medical Practice Acts: Contracts to Pay for Medical Services Rendered by Physicians Selected by Corporation as the Corporate Practice of Medicine.—The state of California, on the relation of the state board of medical examiners, brought quo warranto proceedings against the Pacific Health Corporation to determine the right of the corporation to engage in the practice of medicine. From a judgment of the superior court, city and county of San Francisco, holding its activities violative of the medical practice act, the defendant corporation appealed to the Supreme Court of California.

The case was tried on an agreed statement of facts. The corporation was organized for profit under the general corporation law of California. On application of persons in good health, the corporation issued contracts by the terms of which it undertook, for a specified sum, to pay for services rendered to the holders of the contracts by physicians and hospitals and for certain other services. When a contract holder became sick or injured, the corporation advised him from what physician or hospital the services were to be obtained. After the services were rendered, the corporation paid the charges. The corporation kept a list of physicians and surgeons approved by it, and to obtain the benefits of the service the contract holders were required, except as to emergency expenses not exceeding $50, to accept a physician from the list. The corporation advertised its service and solicited the public to purchase its contracts, paying commissions to its soliciting agents.

The defendant corporation admitted that a corporation may not lawfully engage in the practice of medicine but contended

that it did not undertake to perform medical services, only to furnish competent physicians; that the contracts did not contemplate that services were to be performed at the offices of the corporation but elsewhere, and that the physicians were not employed by the corporation on a salary basis nor directed by the corporation but were compensated for actual services after they had been rendered. The corporation's theory was that the physicians were independent contractors and that this fact absolved it of the charge of practicing medicine.

The Supreme Court was unable to agree that the policy of the law may be circumvented by technical distinctions in the manner in which the physicians are engaged, designated or compensated by the corporation. The evils of divided loyalty and impaired confidence, the court pointed out, seem to be equally present whether the physician receives benefits from the corporation in the form of salary or fees. Freedom of choice of physician is destroyed and the elements of solicitation of medical business and lay control of a profession were present whenever the corporation sought such business from the general public and turned it over to a special group of physicians. As was said in *Pacific Employers Ins. Co.* v. *Carpenter*, 10 Cal. App. (2d) 592, 52 P. (2d) 992:

> But we need not quibble here over the use of terms, as it is immaterial whether the appointed practitioners are termed employees, agents, or appointees of the petitioner. The fact remains that petitioner's agreement was to furnish, in consideration of the premium paid by the insured, the services of doctors and dentists who were to be appointed, engaged, hired, or employed by petitioner for the purpose of furnishing such services. Any such agreement is clearly condemned as unlawful and against public policy . . .

The corporation stressed the effect that an adverse decision might have on other organizations and activities. The court's attention was directed to certain data from medical and lay sources in support of a movement for group medicine and health insurance, and the court was told that a decision against the corporation would outlaw all fraternal, religious, hospital, labor and other similar benevolent organizations furnishing medical services to members. The Supreme Court found this argument wholly unconvincing. The question of the effect of the decision on other organizations, the court said, was not squarely before the court and the information in the record as to their character and activities was meager and unsatisfactory. The court pointed out that the theory of applying the holding of the present case to such philanthropic associations as those mentioned apparently did not exist in the minds of the directors of such associations, nor had it been suggested that the public authorities contemplated any attack on them. This illusory apprehension was expressed, the court said, by the defendant corporation alone in an attempt to bolster up its case by bringing it within the general class of associations furnishing medical or health benefits which have been tacitly approved for generations. A most obvious and to the court a fundamental distinction must be made between the corporation and these other institutions. In nearly all of them, the medical service is rendered to a limited and particular group as a result of cooperative association through membership in the fraternal or other association, or as a result of employment by some corporation which has an interest in the health of its employees. The public is not solicited to purchase the medical services of a panel of physicians and the physicians are not employed or used to make profits for stockholders. In almost every case the institution is organized as a nonprofit corporation or association. Such activities, the court pointed out, are not comparable to those of a private corporation operated for profit, and since the principal evils attendant on the corporate practice of medicine spring from the conflict between the professional standards and the obligations of the physicians and the profit motive of the corporation employer, the objections of policy do not apply to nonprofit institutions.

The corporation questioned whether the time has come, as indicated by the movement for health insurance and group medicine, to reverse the long settled policy against corporate medical practice and declare it legal and proper. A simple answer would be, the court said, that the few extracts from the opinions of writers contained in the briefs furnished no evidence to the court whatever of a widespread change in social point of view sufficient to repudiate the existing law of practically all the states. All that the court had before it was proof of a controversy between medical men, sociologists and others as to the future course of medical practice. The desirability of present methods and the suggested reforms, including various kinds of insurance and group treatment, have been hotly debated. Public policy may change, the court observed, and doubtlessly where statutes do not cover the field the court may follow such changes, but the court must in such case declare as the public policy the social view of people generally and not merely its own private choice among hopelessly conflicting views of desirable reform of settled practices or principles in the field. In the present circumstances, the court said, there can be no true declaration by a court that a change in social point of view now requires the abandonment of the rule against corporate practice of medicine. Such a drastic change should come from the legislature after the full investigation and debate which legislative organization and methods permit. Though certainly aware of the controversy, and with presumed knowledge of the court decisions of California preventing corporate practice, the legislature, the court observed, thus far has not acted.

The court observed, in conclusion, that an admission of the desirability of some form of health insurance or group medicine by no means requires approval of the activities of the defendant corporation. To the court it seemed perfectly possible to bring adequate medical service to the vast numbers of persons who now can ill afford it by some means which will protect both the profession and the public from the evils of corporate control of the practitioner.

The judgment of the trial court, declaring the activities of the corporation violative of the medical practice act, was therefore affirmed. A petition to the United States Supreme Court for a writ of certiorari was denied.—*People ex rel. State Board of Medical Examiners v. Pacific Health Corporation, Inc. (Calif.), 82 P. (2d) 429; 59 S. Ct. 463.*

Society Proceedings

COMING MEETINGS

American Association for the Study of Neoplastic Diseases, Washington, D. C., Sept. 7-9. Dr. Eugene R. Whitmore, 2139 Wyoming Ave. N.W., Washington, D. C., Secretary.

American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 7-9. Dr. James R. Bloss, 418 Eleventh St., Huntington, W. Va., Secretary.

American Association of Railway Surgeons, Chicago, Sept. 11-13. Dr. Daniel B. Moss, 547 West Jackson Blvd., Chicago, Secretary.

American Congress of Physical Therapy, New York, Sept. 5-8. Dr. Richard Kovacs, 2 East 88th St., New York, Secretary.

American Roentgen Ray Society, Chicago, Sept. 19-22. Dr. Carleton B. Peirce, Royal Victoria Hospital, Montreal, Can., Secretary.

Colorado State Medical Society, Colorado Springs, Oct. 4-7. Mr. Harvey T. Sethman, 537 Republic Bldg., Denver, Executive Secretary.

Idaho State Medical Association, Boise, Aug. 23-26. Dr. J. N. Davis, 204 Fourth Avenue East, Twin Falls, Secretary.

Kentucky State Medical Association, Bowling Green, Sept. 11-14. Dr. Arthur T. McCormack, 620 South Third St., Louisville, Secretary.

Michigan State Medical Society, Grand Rapids, Sept. 18-22. Dr. L. Fernald Foster, 311 Center Ave., Bay City Secretary.

Mississippi Valley Medical Society, Burlington, Iowa, Sept. 27-29. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

National Medical Association, New York, Aug. 14-18. Dr. John T. Givens, 1108 Church St., Norfolk, Va., General Secretary.

Nevada State Medical Association, Reno, Sept. 22-23. Dr. Horace J. Brown, 120 North Virginia St., Reno, Secretary.

North Pacific Society of Internal Medicine, Vancouver, B. C., Sept. 1-2. Dr. Lester J. Palmer, 1115 Terry Ave., Seattle, Secretary.

Oregon State Medical Society, Gearhart, Sept. 6-9. Dr. M. L. Bridgeman, 1020 S.W. Taylor St., Portland, Secretary.

Pennsylvania, Medical Society of the State of, Pittsburgh, Oct. 2-5. Dr. Walter F. Donaldson, 500 Penn Ave., Pittsburgh, Secretary.

Rocky Mountain Medical Conference, Salt Lake City, Sept. 5-7. Mr. W. H. Tibbals, 610 McIntyre Bldg., Salt Lake City, Secretary.

Utah State Medical Association, Salt Lake City, Sept. 5-7. Dr. D. G. Edmunds, 610 McIntyre Bldg., Salt Lake City, Secretary.

Virginia, Medical Society of, Richmond, Oct. 2-5. Miss Agnes V. Edwards, 1200 East Clay St., Richmond, Secretary.

Washington State Association, Spokane, Aug. 28-30. Dr. V. W. Spickard, 1305 Fourth Ave., Seattle, Secretary

Wisconsin, State Medical Society of, Milwaukee, Sept. 13-15. Mr. J. G. Crownhart, 119 East Washington Ave., Madison, Secretary.

Wyoming State Medical Society, Salt Lake City, Utah, Sept. 5-7. Dr. M. C. Keith, 156 South Center St., Casper, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1929 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Ophthalmology, St. Louis

22: 595-712 (June) 1939

Gamma of Orbit. M. Fine, San Francisco.—p. 595.
Lectures on Motor Anomalies: X. Supranuclear Paralyses. A. Bielschowsky, Hanover, N. H.—p. 603.
Tonometry and Unusual Cases of Glaucoma. E. Jackson, Denver.—p. 614.
*Frequency of Blinking as Clinical Criterion of Ease of Seeing. M. Luckiesh and F. K. Moss, Cleveland.—p. 616.
Fusospirochetal Infection of Eye and Orbit. G. L. Walker, Iowa City.—p. 622.
Aniseikonia: Study of 836 Patients Examined with Ophthalmo-Eikonometer. C. Berens and M. Loutfallah, New York.—p. 625.
Adrenal Neuroblastoma and Its Ocular Symptoms: Case Report with Autopsy. H. S. Kuhn, Hammond, Ind.—p. 642.
Cultivation in Vitro of Human Conjunctival and Corneal Epithelium. P. Thygeson, New York.—p. 649.
Testing Fitness for Night Flying: Speed of Change of Adjustment of Eyes for Intensity of Light and Distance of Object. C. E. Ferree and G. Rand, Baltimore.—p. 655.

Frequency of Blinking as Criterion of Visual Ease.—Luckiesh and Moss discuss the periodic movements of the eyelids as a criterion of ease of seeing and as a clinical method for appraising ocular comfort. They have confirmed the assumption that blinking is associated with effort and fatigue by observing the frequency of blinking during the first and last five minute periods of an hour of continuous reading. The experimental conditions involved the reading of interesting material under three different levels of illumination by eleven adults possessing normal or near normal vision. The frequency of blinking was higher during the last five minute period of reading than during the first period under all illuminations. The rate of blinking during the last five minute period decreased as the task of reading was made easier by higher levels of illumination. Thus it appears that the frequency of blinking is definitely correlated with both the duration and the severity of the visual task. An increase in the frequency of blinking invariably occurs when the conditions for seeing are made more unfavorable, which involve (1) the fatiguing effects of prolonged voluntary activity of the extrinsic muscles, (2) the distraction of a bright peripheral image during reading, (3) the fixation and recognition of minute details, (4) an unusual relationship between accommodation and convergence owing to the red background of the reading matter and (5) perceptual and fixational difficulties arising from closely spaced lines of print. Hence it follows that the rate of blinking is intimately related to various and complex psychophysiologic factors involved in seeing, thus empirically confirming the conclusions of Ponder and Kennedy. Therefore blinking is an extremely sensitive criterion of ease of seeing and the authors have used it as a criterion for appraising ocular strain and fatigue arising from uncorrected or improperly corrected refractive errors of the human eye. The number of blinks occurring during five minute periods of reading is given for thirty subjects wearing plus 0.50 diopter spheres, plano lenses and minus 0.50 diopter spheres in addition to the usual correction, if any. The minimal frequency of blinking occurred with plano lenses in addition to the usual corrections, if any. Quantitatively, the frequency of blinking was increased about 42 per cent by the addition of the convex spheres and about 37 per cent for the concave spheres during a five minute period of reading. The highest rate of blinking was not obtained with the plano lenses in any one of the thirty cases studied. This fact represents additional evidence that the observed differences in blinking are due to differences in ocular comfort rather than to uncontrolled factors or chance.

American Journal of Physiology, Baltimore

126: 215-416 (June) 1939. Partial Index

Induction of Estrous Behavior in Anestrous Cats with the Follicle Stimulating and Luteinizing Hormones of Anterior Pituitary Gland. H. B. Friedgood, Boston.—p. 229.
Variations in Intramuscular Pressure During Postural and Phasic Contraction of Human Muscle. Frances A. Hellebrandt, Eleanor Fielding Crigler and L. E. A. Kelso, Madison, Wis.—p. 247.
*Effect of Avitaminosis A on Human Blood Picture. O. D. Abbott, C. F. Ahmann and M. R. Overstreet, Gainesville, Fla.—p. 254.
Action of Lead on Phosphocreatine in Muscular Paralysis of Lead Poisoning. S. E. Steiman, Boston.—p. 261.
Depressant Action of Strychnine on Superior Cervical Sympathetic Ganglion and on Skeletal Muscle. A. Lanari and J. V. Luco, Boston.—p. 277.
Quantitative Relation Between Reactive Hyperemia and the Myocardial Ischemia Which It Follows. L. N. Katz and E. Lindner, Chicago.—p. 283.
Specificity of Thrombin Action. A. L. Copley, Basle, Switzerland.—p. 310.
Bile Pigment and Hemoglobin Interrelation in Anemic Dogs. W. B. Hawkins and A. C. Johnson, Rochester, N. Y.—p. 326.
Plasma Potassium Content of Cardiac Blood at Death. J. Scudder, Margaret E. Smith and C. R. Drew, New York.—p. 337.
Sodium Chloride and Diabetes Insipidus. H. G. Swann, Chicago.—p. 341.
Effects of Renin, Pitressin and Pitressin and Atropine on Renal Blood Flow and Clearance. A. C. Corcoran and I. H. Page, Indianapolis.—p. 354.
Relation of Adrenal Cortex to Male Reproductive System. I. Gersh and A. Grollman, Baltimore.—p. 368.
Respiratory Resistance, Oil-Water Solubility and Mental Effects of Argon, Compared with Helium and Nitrogen. A. R. Behnke and O. D. Yarbrough, Washington, D. C.—p. 409.

Effect of Avitaminosis A on Blood.—Abbott and his co-workers made differential leukocyte counts on the blood of 157 individuals whose diets and symptoms indicated a vitamin A deficiency. The blood picture of all the subjects showed several variations from normal hematologic standards. Among these were a decrease in total leukocytes and polymorphonuclears, an increase in juveniles and large lymphocytes, and degeneration, especially of the granulocytes. This blood picture is similar to that of rats fed a diet deficient in vitamin A and, as in the case of the rats, the administration of large amounts of vitamin A brought about a gradual improvement in symptoms and in a few weeks the differential count was within the normal range. From this work it was concluded that the differential leukocyte count is of diagnostic value in vitamin A deficiency in man.

American Journal of Surgery, New York

44: 533-726 (June) 1939

Surgical Treatment of Essential Hypertension. P. G. Flothow, Seattle.—p. 535.
Hydatidiform Mole: Analysis and Follow-Up of Twenty-Four Cases. M. V. Armstrong, Brooklyn.—p. 544.
Granuloma Inguinale (Venereum) in the Female. R. Torpin, R. B. Greenblatt and E. R. Pund, Augusta, Ga.—p. 551.
Tendon Injuries: Their Classification and Early Treatment. D. Goldblatt, New York.—p. 557.
*Visceral Complications in Tuberculosis of Bones and Joints. H. R. Landmann, New York.—p. 569.
New Closed Method of Treating Supracondylar Fractures of Elbow. E. L. Jewett, Orlando, Fla.—p. 572.
Submucous Hemorrhoidectomy. A. S. Calman, New York.—p. 577.
Renal Hydatidosis. L. A. Surraco, Montevideo, Uruguay.—p. 581.
Injection Therapy of Hydrocele and Spermatocele. A. H. Milbert, New York.—p. 587.
Direct and Indirect Hernia in Light of Newer Interpretation of Anatomy of Anterior Abdominal Wall. M. Cherner, Philadelphia.—p. 593.
Ten Years' Experience with Leg Ulcers in the Old Age Group. M. Baruch, S. T. Glasser and J. Rosenthal, New York.—p. 601.
*Concerning the Surgical Physiology of Duodenal Ulcer. V. G. Burden, Philadelphia.—p. 608.
Exploratory Laparotomy. W. T. Coughlin, St. Louis.—p. 614.
Sclerotherapy for Pilonidal Cyst. H. I. Biegeleisen, New York.—p. 622.
Use of Alkyldimethylbenzyl-Ammonium Chloride in Injury. L. T. Wright and R. S. Wilkinson, New York.—p. 626.

Visceral Complications in Osseous Tuberculosis.—Landmann studied the nature of visceral involvement in 159 cases of tuberculosis of the bones and joints admitted to the Hospital for Joint Diseases and the Mount Sinai Hospital during 1932 to 1936 inclusive. Seventy-two cases involved the spine, forty-four cases involved the knee, eighteen cases occurred in the hip joints and twenty-five involved other joints. Ten of the 159 cases showed evidence of visceral complications. Most of the visceral complications were secondary tuberculosis infections or possibly foci present without symptoms before the onset of perceptible bone and joint manifestations. The complicating infection involved the genito-urinary system in eight

cases, the liver in one and Addison's disease was present in one. There were four cases of proved renal tuberculosis and one case of proved tuberculous epididymitis. The repeated demonstration of secondary genito-urinary involvement in skeletal tuberculosis should suggest the advisability of examining the urine of all patients suffering from tuberculosis of the bones and joints at regular intervals for tubercle bacilli, so that lesions might be discovered early. Since early renal tuberculosis gives no lead to the examiner because of lack of symptoms, repeated examination of the urine should be done as a routine. Many progressive cases of renal tuberculosis or tuberculosis of the ureter and bladder could be thereby anticipated and proper measures instituted.

Surgical Physiology of Duodenal Ulcer.—Burden believes that many of the clinical features of duodenal ulcer can be explained by the activity of the pyloric sphincter. It may cause the typical symptoms of ulcer when no ulcer is present, since the ulcer itself does not cause the symptoms which identify its presence. Dysfunction of the pyloric sphincter is one and hyperacidity is the other main factor in the etiology of duodenal ulcer. The normal stomach regulates its own acidity. Failure of this control means the development and maintenance of a duodenal ulcer. The pyloric sphincter because of spasm or failure to relax becomes a potent hindrance to the regurgitation of alkaline duodenal contents into the stomach. Of the two factors concerned in the etiology and maintenance of duodenal ulcer, dysfunction of the pyloric sphincter alone is amenable to direct attack. Its function can be abolished permanently by removing the anterior half of the sphincter without opening into the duodenum or stomach. This procedure has been carried out with lasting success in cases of duodenal ulcer.

American Review of Tuberculosis, New York

39: 683-840 (June) 1939

Pulmonary Tuberculosis in Second Decade of Life: I. Its Development and Fatality. D. Zacks, Boston.—p. 683.
*14.: II. Its Treatment and Prognosis. D. Zacks, Boston.—p. 703.
*Diabetes and Pulmonary Tuberculosis, with Special Reference to Lipid Content of Diabetic Lungs. H. F. Root and W. R. Bloor, Boston.—p. 714.
Oral Tuberculosis. J. C. Bryant, Oak Terrace, Minn.—p. 738.
Bilateral Tuberculous Pleurisy with Effusion: Analysis of Fourteen Cases. G. C. Wilson, Wallingford, Conn.—p. 745.
Erythrocyte Sedimentation: Its Practical Value in Management of Pulmonary Tuberculosis. T. De Cecio and B. J. Elwood, Jersey City, N. J.—p. 748.
Epidemiologic Aspects of Negative Tuberculin Reaction. M. Paretsky, Los Angeles.—p. 754.
Detection of Tuberculosis in Group Surveys. P. T. Knies, Columbus, Ohio.—p. 766.
Tuberculosis Survey of an Entire Community. R. Davies and C. A. Scherer, Nopeming, Minn.—p. 778.
Effects of Ultraviolet Radiation on Tubercle Bacilli. K. C. Smithburn and G. I. Lavin, New York.—p. 782.
Vitamin C and Immunity in Tuberculosis of Guinea Pigs. F. H. Heise and W. Steenken Jr., Trudeau, N. Y.—p. 794.
Pathologic Changes in Pulmonary Tuberculosis in Jamaican Negroes. C. W. Wells, Kingston, Jamaica, British West Indies.—p. 796.

Treatment and Prognosis of Tuberculosis in Children.—Zacks observed the effect of treatment and prognosis, as measured by x-ray examination, on 536 children in the second decade of life with pulmonary tuberculosis who were followed for an average of four years. The most pertinent observation was that the treated boys give a mortality rate of 4.2 per cent a year, the untreated 3.2 per cent a year. The mortality for the treated girls is 7.1 per cent, for the untreated 5 per cent. This result can be explained only on the basis of selection, as the patients with a more advanced condition were naturally the first to accept treatment. The author's conclusions are that bed rest alone in a sanatorium does not modify the course of spreading tuberculous lesions to an appreciable degree and does not reduce the mortality from these lesions. Bed rest alone or bed rest with pneumothorax has not appreciably affected the mortality in advanced bilateral lesions or lesions of minimal extent that are allowed to progress too far without early collapse therapy. Collapse therapy in advanced unilateral lesions tends at least to prolong life and it may also reduce the mortality. Evidence seems to indicate that early collapse therapy may reduce the fatality rate of early asymptomatic lesions that show a tendency to spread. A final answer on this point cannot be given without at least five more years of observation. In the second decade of life, the prognosis for soft early lesions is uncertain for at least ten years. Lesions that progress ultimately do poorly—those that retrogress on the whole do well. Retrogressive lesions should be observed by serial roentgenograms until definite stabilization is evident by calcification, by strandlike fibrosis or both.

Diabetes and Pulmonary Tuberculosis.—Root and Bloor assert, from a study of the various etiologic factors in 364 cases of diabetes with pulmonary tuberculosis, that the disturbed nutrition in diabetes is next in importance to contact with an open case of tuberculosis. Pulmonary tuberculosis developed in juvenile diabetic patients, whose diabetes began at or before the age of 20 years, more than twelve times as frequently as among pupils in the Massachusetts grade and high schools. Of seventy-three patients recovering from diabetic coma between February 1929 and November 1932, pulmonary tuberculosis developed in thirteen of them within five years. The incidence of pulmonary tuberculosis in adult diabetes does not show a decrease in rate corresponding with the general decrease in tuberculosis mortality in the community. Pulmonary tuberculosis followed the onset of diabetes in 83 per cent of the cases. The main features in 126 necropsies on diabetic patients with pulmonary tuberculosis were many healed foci, a tendency for the formation of tough, fibrous, pleural adhesions and a high frequency of caseating lesions with cavitation. Chemical analysis of the lungs of tuberculous patients with diabetes showed strikingly lower concentrations of phospholipid and lipid than in nondiabetic patients. Seven new cases of the diagnosis of tuberculosis in the minimal stage are reported. Among 258 fatal cases the average duration of diabetes to death has increased from 5.4 to 10.1 years and the duration of pulmonary tuberculosis from 2.7 to four years. Diabetic patients make excellent subjects for pneumothorax and thoracoplasty. Routine x-ray examination of every diabetic patient's chest is recommended.

Annals of Surgery, Philadelphia

109: 881-1050 (June) 1939

Antiseptic and Detoxifying Action of Zinc Peroxide on Certain Surgical Aerobic, Anaerobic and Micro-Aerophilic Bacteria. Balbina A. Johnson and F. L. Meleney, New York.—p. 881.
Benign and Malignant Lesions of Male Breast. J. S. Horsley Jr., Richmond, Va.—p. 912.
Plasma Cell Mastitis. J. S. Rodman and Helen Ingleby, Philadelphia.—p. 921.
Nonpenetrating Intra-Abdominal Injury. F. W. Bailey, St. Louis.—p. 931.
Studies on Reaction of Peritoneum to Trauma and Infection. F. A. Coller and H. Brinkman, Ann Arbor, Mich.—p. 942.
*Appendicocecostomy in Treatment of Peritonitis. T. B. Reeves, Greenville, S. C.—p. 955.
Unusual Spleen Cases. A. P. Jones, Roanoke, Va.—p. 960.
Conservative Pelvic Surgery. W. F. Shallenberger, Atlanta, Ga.—p. 970.
Genital Tuberculosis and Pregnancy, with Special Reference to Tubal Gestation. L. R. Wharton and C. S. Stevenson, Baltimore.—p. 976.
Injury to Ureters During Pelvic Operations. Q. U. Newell, St. Louis.—p. 981.
Femoral Hernia: Report of Ninety Operations. R. D. McClure and L. S. Fallis, Detroit.—p. 987.
*Theory and Practical Use of Z Incision for Relief of Scar Contractures. J. S. Davis and E. A. Kitlowski, Baltimore.—p. 1001.
Utilization of Temporal Muscle and Fascia in Facial Paralysis. J. B. Brown, St. Louis.—p. 1016.
Treatment of Sciatic Syndrome by Iliotibial Fascial Band Section. C. C. Green and J. R. Gondy, Houston, Texas.—p. 1024.
Neurologic Aspects of Low Back Pain and Sciatica. E. F. Fincher, Atlanta, Ga.—p. 1028.

Appendicocecostomy in Treatment of Peritonitis.—During the last six or seven years, Reeves has performed a cecostomy or appendicocecostomy in fifty-two of his worst cases of ruptured appendicitis, in most of which there was a general peritonitis. He has not employed this operation in cases of recent rupture although he knows of no contraindication for doing it in such cases, nor has he used it in any case in which there was a walled-off abscess. There were six deaths in the fifty-two cases, a mortality of approximately 12 per cent, which compares favorably with other statistics. All the cecostomies closed primarily in from two to three weeks except in one case, in which the fistula was closed two months later.

Z Incision for Relief of Scar Contractures.—Davis and Kitlowski state that the operative procedure of the Z plastic maneuver, based on the transposition of two triangular flaps,

is simpler than other methods for relaxing scar contractures. Tissues which would otherwise be discarded are advantageously utilized. The appearance of an area relaxed by this method compares favorably with that of other methods. Additional scarring of unscarred areas is avoided. Contractions can be permanently relieved by this method which would be difficult or not practical to correct by skin grafting. Satisfactory and effective relaxation can be accomplished in contracted scars with bridles, webs or grooves. The suture line after transposition is as a rule Z shaped, but the Z is turned through approximately 90 degrees and the central line of the original Z lies transversely across the line of the scar pull and prevents recontraction. The success of the method depends on the presence of lax tissue which can be drawn in from the sides. In many instances the authors have been able to restore function and return patients, either partially or completely incapacitated, to their ordinary occupations. They have used the incision for many years on every part of the body and they find it one of the most generally helpful maneuvers.

Archives of Internal Medicine, Chicago

63: 1017-1238 (June) 1939

Treatment of Massive Hemorrhage Due to Peptic Ulcer. J. S. LaDue, Minneapolis.—p. 1017.
Critical Evaluation of Gastric Antacids. W. L. Adams, Albany, N. Y. —p. 1030.
Changes in Acid-Base Balance During Alkali Treatment for Peptic Ulcer: Clinical Analysis of Alkalosis in Twenty-Eight Patients. C. W. Eisele, Chicago.—p. 1048.
*Staphylococcic Septicemia: Review of Thirty-Five Cases, with Six Recoveries, Twenty-Nine Deaths and Sixteen Autopsies. T. H. Mendell, Philadelphia.—p. 1068.
Cortical Necrosis of Kidney Following Tonsilitis: Report of Case. R. G. Weaver and E. von Haam, Columbus, Ohio.—p. 1084.
*Excretion of Ascorbic Acid in Relation to Saturation and Utilization with Some Diagnostic Implications. M. A. Spellberg and R. W. Keeton, Chicago.—p. 1095.
Incidence of Pulmonary and Extrapulmonary Tuberculosis in Anthracite Coal Miners. A. C. Cohen, White Haven, Pa.—p. 1117.
Relation of Hereditary Pattern to Clinical Severity as Illustrated by Peroneal Atrophy. W. Allan, Charlotte, N. C.—p. 1123.
Clinical Recognition of Tuberculosis of Major Bronchi. A. G. Cohen and H. Wessler, New York.—p. 1132.
Oscillometry in Diagnosis of Arteriosclerosis of Lower Extremities: New Method of Application. L. N. Atlas, Cleveland.—p. 1158.
Periarteritis Nodosa. A. W. Harris, Dallas, Texas; G. W. Lynch and J. P. O'Hare, Boston.—p. 1163.
Roentgen Diagnosis of Mural Thrombi. L. H. Berk, New York.—p. 1183.
Blood: Review of Recent Literature. C. C. Sturgis, R. Isaacs, S. M. Goldhamer and F. H. Bethell, Ann Arbor, Mich.—p. 1190.

Staphylococcic Septicemia.—Mendell discusses a series of thirty-five cases of staphylococcic septicemia seen over a period of eight years. There were six recoveries, twenty-nine fatalities and sixteen postmortem examinations. The incidence, sex, age, source of infection, duration of the disease, laboratory observations, complications observed clinically as contrasted with those seen at postmortem study, treatment and prognosis are discussed. It is shown that complications occur early in the course of the disease and exist more frequently than can be discovered clinically. With no specific treatment available, surgical eradication of the source of infection, with prompt removal of metastatic foci of suppuration as they occur, plus repeated immunotransfusions is the basis for any successful treatment. Three cases in which recovery was obtained are reported in detail to emphasize these features of the disease.

Excretion, Saturation and Utilization of Ascorbic Acid.—According to Spellberg and Keeton, persons normal from a dietary point of view show a prompt rise in urinary excretion and blood concentration of ascorbic acid, with rapid "saturation," when large doses of the acid are administered by mouth. "Exhausted" patients show a delay in saturation, but their blood concentration rises above 1 mg. per hundred cubic centimeters of blood before a great rise in the urinary excretion occurs. The diagnostic features of scurvy seem to be a lowered renal threshold for ascorbic acid, extreme depletion of the body stores and an unusual delay of saturation as evidenced by urinary excretion. There seems to be increased utilization of ascorbic acid in diseases accompanied by increase in oxidative processes or in cellular proliferation, e. g. (1) malignant tumor, (2) hyperthyroidism and (3) leukemia. Alkali medication does not interfere with absorption of ascorbic acid in cases of peptic ulcer. Treatment by Sippy diets when prolonged leads to depletion of the stored ascorbic acid. Patients with clinical asthma show no abnormality of storage. Large doses of ascorbic acid given intravenously or by mouth have no ameliorating effect on the attacks. Hepatic damage in portal cirrhosis does not interfere with the storage of ascorbic acid. Ascitic fluid contains the same concentration of ascorbic acid as blood plasma.

Archives of Neurology and Psychiatry, Chicago

42: 1-188 (July) 1939

*Studies in Mongolism: III. Pituitary Body. C. E. Benda, Wrentham, Mass.—p. 1.
Visual Disturbances Associated with Tumors of Temporal Lobe. H. S. Sanford, Detroit, and H. L. Bair, Rochester, Minn.—p. 21.
Vascular Pattern of Certain Intracranial Neoplasms: Studies with Benzidine Stain. A. L. Sahs, Iowa City, and L. Alexander, Boston. —p. 44.
Physiologic Significance of Creatinine Coefficient and Creatine Tolerance Test: Critical Review. H. H. Beard and E. J. Jacob, New Orleans. —p. 67.
*Hypothalamic Nuclei in Heat Stroke, with Notes on Central Representation of Temperature Regulation. L. O. Morgan and A. R. Vonderahe, Cincinnati.—p. 83.
Studies of Spinal Fluid in Cases of Injury to the Head: Effects of Drainage, Isotonic Fluids, Morphine and Soluble Phenobarbital U. S. P. on Cerebrospinal Fluid Pressure. E. S. Gurdjian, J. E. Webster and C. J. Sprunk, Detroit.—p. 92.
Effect of Benzedrine Sulfate in Treatment of Psychosis with Post-encephalitic Parkinsonism. L. Bernikoff, Secaucus, N. J.—p. 112.
Prepsychotic Measurements of Physical and Mental Growth in Case of Juvenile Dementia Paralytica. G. E. Gardner, Boston.—p. 121.
Aneurysm of Vertebral Artery. P. Bassoe, Chicago.—p. 127.

Pituitary Body in Mongolism.—Benda examined microscopically the pituitary bodies of thirteen supposedly mongoloid patients and of one case of premature birth. The definite alterations peculiar to mongolism consisted of an increase of eosinophilic cells and a deficiency of basophilic and chief cells. In analyzing these alterations the author believes that, because the size of the pituitary is not increased and no signs of eosinophilic hyperactivity are found, the absence or deficiency of basophilic cells appears to be the most important observation. There are many indications that mongolism is the result of a morphokinetic failure and is due to an endocrine disturbance. The key to the general disorder seems to be a particular pituitary deficiency, which may be due to a pituitary deficiency of the mother during pregnancy. The advanced maternal age, frequently observed in cases of mongolism, and other factors indicate that the maternal organism is not apt to adjust itself to a new pregnancy.

Hypothalamic Nuclei in Heat Stroke.—The nuclei of the hypothalamus in thirteen patients who died of heat stroke were studied by Morgan and Vonderahe and compared with the nuclei of the hypothalamus in five control brains from patients who died of a variety of causes (malignant hypertension, gunshot wound in the back, skull fracture, pulmonary tuberculosis and mercury bichloride poisoning). Eleven of the thirteen patients with heat stroke were men. Twelve of the thirteen were 50 years of age or older. In all twelve cases in which complete necropsy was performed, heat stroke was associated with some pathologic process tending to produce degenerative changes in the central nervous system. In nine it was associated with generalized vascular sclerosis, in two with syphilis and in one with chronic alcoholism. The nucleus paraventricularis in cases of heat stroke presented an average cell loss of 27 per cent; of the cells that remained, an average of 77 per cent were normal. The large cells of this nucleus were principally affected as compared with diabetes mellitus, in which the small and medium sized cells were principally affected. The nucleus tuberis lateralis presented an average cell loss of 40 per cent; of the cells that remained, an average of 47 per cent were normal. In the control cases, pathologic alterations frequently occurred in the cells of this nucleus, the average of normal cells being 65 per cent. The nucleus tuberomamillaris presented no decisive alteration in cell counts. There was, however, general and constant pathologic change, with an average of only 27 per cent of cells remaining normal. The basal optic ganglions (nucleus supra-opticus) and the cells of the substantia grisea did not present sufficiently significant constant cell loss. Chromatolysis, while variable, was of a sufficient degree so that the heat-regulating functions of these structures were considered. The most likely interpretation that the authors place on their observations is that the lateral nuclei of the tuber and a portion of the paraventricular nuclei are primarily concerned

with elimination of heat. The nucleus tuberomamillaris, which is acutely affected in both experimental fever and heat stroke, is probably concerned with heat production (metabolism). If, then, in cases of heat stroke the mechanisms for heat elimination are weakened it is possible that these mechanisms break down when subjected to an extremely high environmental temperature. These mechanisms having broken down, the normal balance between heat production and heat elimination is destroyed. This may remove a part of the normal checks or inhibitions from the mechanisms for heat production so that the total metabolism is accelerated rather than inhibited.

Connecticut State Medical Society Journal, Hartford

3: 265-328 (June) 1939

Surgical Treatment of Hypertension: Observations—Thirty-Eight Patients Selected for Surgical Therapy. F. Glenn, New York.—p. 268.

Use of Drugs in Treatment of Essential Hypertension. D. Ayman, Boston.—p. 270.

*Results from Colloidal Aluminum Hydroxide in Peptic Ulcer Therapy: An Eighteen Months Survey at the Hartford Hospital, Hartford, Conn. B. B. Whitcomb, New Haven.—p. 272.

The U Wave of the Human Electrocardiogram. L. H. Nahum, New Haven.—p. 275.

Huge Syphilitic Aneurysm: Case Report. J. H. Foster, Waterbury.—p. 276.

Neurologic Manifestations in Pernicious Anemia: Report of Five Cases. T. S. Evans and S. Spinner, New Haven.—p. 278.

Life Insurance: A Design for Living. E. H. Snow, Hartford.—p. 284.

Colloidal Aluminum Hydroxide for Peptic Ulcer.—Whitcomb compares the results of treating fifty cases of peptic ulcer with colloidal hydroxide, forty-five with the Sippy regimen and nine by means of various other medical methods. When compared with the Sippy regimen the use of colloidal aluminum hydroxide reduced the length of hospitalization for the series by 560 hospital days. It promoted a more rapid and definite healing process as demonstrated roentgenologically, symptomatic relief and lack of recurrences. The latter feature may be due in a large part to the simplicity of this method of treatment, which is an advantage over the more detailed Sippy regimen and therefore more likely to be followed after the patient has been discharged. Other advantages are the increased activity permitted during treatment and the wider latitude in diet, which permits the free use of essential foods. Of the patients treated with colloidal aluminum hydroxide healing was demonstrated at an earlier date in those receiving the treatment by the constant drip method. This method appeared more effective in cases in which there was a high acid curve. The method was preferred by the refractory and those patients whose condition required more drastic methods—as in one case showing by x-ray examination a chronically indurated postpyloric ulcer with a marked obstruction and twenty-four hour residue. In twenty-one of the admissions reviewed, symptoms were not relieved by Sippy treatment. In nine, aluminum hydroxide was subsequently given with prompt relief of symptoms. In another case of Sippy failure, aluminum hydroxide therapy, strictly followed for one week, also failed to relieve severe pyrosis following several hemorrhages. This was the only case of the series in which a surgical operation following failure to control the symptoms by colloidal aluminum hydroxide also failed to control the symptoms. Seven of the cases that were treated effectively by aluminum hydroxide were recurrences following surgery. There were no recurrences in the cases treated by aluminum hydroxide as compared to 13.5 per cent of the Sippy cases. The failure to control symptoms during treatment was four times as great among those on the Sippy regimen.

Georgia Medical Association Journal, Atlanta

28: 221-262 (June) 1939

Suggestions for Use of Anesthetics and Analgesics in General Medical Practice. J. S. Lundy, Rochester, Minn.—p. 221.

St. Louis Session of the A. M. A. Considers Wagner Bill. C. W. Roberts, Atlanta.—p. 226.

Labor: Rotation and Delivery of Fetal Head by Use of Suction Cup Instead of Forceps: Report of Cases. R. Torpin, Augusta.—p. 230.

Crossed Ectopia of Kidney: Report of Case. W. L. Bazemore and W. R. Golson, Macon.—p. 235.

Intrapleural Pneumonolysis as Adjunct to Pneumothorax in Treatment of Pulmonary Tuberculosis. C. C. Garver, Atlanta.—p. 236.

Arthritis: Treatment by Hyperpyrexia. H. M. Davison, M. I. Lowance and W. R. Crowe, Atlanta.—p. 243.

Journal of Infectious Diseases, Chicago

64: 193-318 (May-June) 1939. Partial Index

Inclusion Bodies in Scarlet Fever. Jean Broadhurst, Gladys Cameron, M. Estelle MacLean and V. Saurino, New York.—p. 193.

Active and Passive Immunization in Experimental Poliomyelitis. F. B. Gordon, N. P. Hudson and J. A. Harrison, Chicago.—p. 241.

Immunization Against Rabies Using Avirulent Purified Vaccines. F. B. Behrens, L. B. Schweiger, J. F. Barker and J. L. Reeves, Lafayette, Ind.—p. 252.

Survival and Death of Tubercle Bacilli Subjected to Oxygen Restriction. T. S. Potter, Chicago.—p. 261.

Cross Immune Relationship of Various Strains of Plasmodium Cathemerium and Plasmodium Relictum. W. B. Redmond, Chicago.—p. 273.

Use of Experimental Pneumonia in Rats for Evaluation of Therapeutic Procedures. W. J. Nungester and Alice H. Kempf, Ann Arbor, Mich.—p. 288.

Some Chemical and Physical Studies of Staphylococcus Enterotoxin. Ellen Davison and G. M. Dack, Chicago.—p. 302.

Survival of Virus of St. Louis Encephalitis in Rats and Guinea Pigs. Margaret G. Smith, St. Louis.—p. 307.

Use of Gastric Mucin in Diagnosis of Epidemic Meningitis. S. E. Sulkin, St. Louis.—p. 310.

Attempted Cultivation of Donovan Bodies from Granuloma Inguinale. B. Carter, C. P. Jones and W. L. Thomas, Durham, N. C.—p. 314.

Journal of Pediatrics, St. Louis

14: 695-844 (June) 1939

Sepsis of the Newborn Infant. M. L. Blatt and A. A. Wolf, Chicago.—p. 695.

Staphylococcic Pneumonia: Clinical, Pathologic and Bacteriologic Study. A. Kanof, B. Kramer and M. Carnes, Brooklyn.—p. 712.

Irradiated Evaporated Milk as Food for Infants: Study of Growth, Elimination, Protection from Rickets and Morbidity in Upper Respiratory Infections in Comparative Groups Fed on Irradiated and Non-irradiated Evaporated Milk. C. G. Grulee, H. N. Sanford and M. Lewison, Chicago.—p. 725.

*Prevention of Purulent Otitis Media in Infants. H. Bakwin and H. Jacobziner, New York.—p. 730.

Repeated Glucose Tolerance Tests in Children. H. J. John, Cleveland.—p. 737.

Cerebral Vascular Lesions Accompanying Sickle-Cell Anemia. J. M. Arena, Durham, N. C.—p. 745.

Tuberculin Patch Test: Comparison with Pirquet and Mantoux Tests. S. B. Weiner and A. Neustadt, New York.—p. 752.

Atropine Intoxication: Its Manifestations in Infants and Children. H. G. Morton, Durham, N. C.—p. 755.

Diagnosis of Congenital Syphilis: Pathognomonic Criteria. W. C. Black, San Diego, Calif.—p. 761.

*Bronchography in Children: Simple Method Accomplished with General Anesthesia. C. W. Lester and E. A. Rovepatine, New York.—p. 780.

*Pectin-Agar Diets in Treatment of Bacillary Dysentery of Infants and Children. M. Winters, C. A. Tompkins and Grace W. Crook, Indianapolis.—p. 788.

Congenital Carcinoma of Thymus with Extensive Generalized Metastases. P. Wasserman, Cincinnati, and J. W. Epstein, Cleveland.—p. 798.

Subcutaneous Emphysema in the Newborn Infant: Case Report. W. McMann and C. W. Purcell, Danville, Va.—p. 805.

A Buccal Oxygen-Ether Catheter. R. Cohen, Louisville, Ky.—p. 807.

The Future of American Pediatrics. W. C. Davison, Durham, N. C.—p. 810.

Prevention of Purulent Otitis Media.—Clinical observation over a period of five years has led Bakwin and Jacobziner to believe that incising an inflamed drum often leads to a purulent discharge in an ear in which, if there were no operative intervention, the infection would subside spontaneously. Furthermore, the results over a period of five years strongly indicate that frequent examinations of the ear, by traumatizing the drum and the canal and by exposing the nasopharynx of the infant to the expired air of the examiner, favor the development of purulent otitis media. In many pediatric hospitals otitis media is treated casually and its management is left to the house officers without adequate supervision by the visiting staff. This attitude is fraught with danger, as it exposes children already ill to the danger and inconvenience of unnecessary paracenteses and purulent otitic discharges. Though disease of the mastoid is uncommon in infants, it does occur and is to be avoided if possible. By careful supervision, strict adherence to a standardized set of indications for myringotomy and the avoidance of too frequent examinations, the incidence of purulent otitis media may be reduced and the danger of disease of the mastoid lessened. The authors state that the results of their study lend no support to the view that delay in incising an ear drum is harmful to the child. When doubt exists, they believe that it is preferable to wait. In acute intestinal intoxication, when a specific relationship to acute purulent otitis media has been hypothesized, the incidence of aural discharge has been reduced to one third during the five years under discussion, with a fall rather than a rise in case fatality from this serious disease.

Bronchography in Children.—As a substitute method for local anesthesia employed in bronchography in conscious children Lester and Rovenstine describe a technic of inhalation anesthesia with nitrous oxide-oxygen, after basal narcosis with tribromethanol in amylene hydrate and the application of a 3 per cent solution of metycaine to the mucous membranes. The method permits the accurate introduction of the contrast medium by way of an endotracheal tube and the removal of most of it after the bronchographic examination is completed. Results after more than one year's trial indicate that the method is relatively safe, pleasant for the patients and time saving, and also that the results have been more satisfactory than with any other technic used.

Pectin-Agar Diets for Bacillary Dysentery.—Winters and his colleagues used a pectin-agar preparation of maltose and dextrin in the treatment of fifty-two cases of bacillary dysentery and twenty-seven cases of infectious gastro-enteritis, probably dysentery, in infants and children. Soft stools were produced within an average of thirty-four hours and a gradual and steady improvement took place in 73.4 per cent of the children. The daily intake averaged from 33 to 52.4 calories per pound, and average weight gains were observed in every group. The mode of action of this therapy is probably both physicochemical and mechanical, with the uronic acids playing an important part. The diet, besides having a definite therapeutic action, is high in calories, well balanced and easily assimilated, and it maintains nutrition while the body has a chance to develop the necessary immunity. The authors find that the pectin-agar diet definitely produces formed stools more quickly with fewer recurrences than other accepted methods, including the apple diet.

Kansas Medical Society Journal, Topeka

40: 229-272 (June) 1939

Preoperative and Postoperative Care of Toxic Goiter. A. S. Jackson, Madison, Wis.—p. 230.
Coronary Occlusion. J. R. Miller, Chicago.—p. 234.
Surgical Treatment of Prostatic Obstruction. A. G. Isaac, Newton.—p. 238.
Pediatric Program for the Family Doctor. M. G. Peterman, Milwaukee.—p. 240.
Primary Sarcoma of Lung with Brain Metastasis. R. C. Ellis, Kansas City.—p. 243.

Maine Medical Association Journal, Portland

30: 123-154 (June) 1939

The Legal Status of the Intern. F. E. Clow, Wolfeboro, N. H.—p. 123.
Poor Patients in Hospital Wards. Sister Ricard, Lewiston.—p. 127.

Military Surgeon, Washington, D. C.

84: 537-640 (June) 1939

Classification of Hypertension: Prognosis and Management. A. W. Adson.—p. 537.
Development of Efficient and Intelligent System of Oral Diagnosis. B. L. Brun.—p. 556.
Sulfanilamide in Treatment of Gonorrhea: Report of Results Obtained in 100 Cases. J. C. Kimbrough.—p. 568.
Electrosurgery in War. G. M. Blech.—p. 577.
Principles of Surgery, Hospitalization and Evacuation of Wounded in the Meuse-Argonne Offensive. H. H. M. Lyle.—p. 580.
Cardiac Arrhythmias and Tachycardias. H. L. Smith.—p. 591.
Misleading Urinalyses. G. O. Haynes.—p. 595.

Minnesota Medicine, St. Paul

22: 363-436 (June) 1939

Pagés' Peridural Anesthesia: Report of 3,826 Cases. V. Ruiz, Buenos Aires, Argentina.—p. 363.
*Treatment of Pneumococcic Meningitis with Sulfanilamide and Specific Serum: Report of Case with Agranulocytosis and Recovery. R. C. Gray, Minneapolis, and B. Adams, Loveland, Colo.—p. 369.
Idiopathic Benign Hypertrophic Pyloric Stenosis in the Adult. F. E. Kibler, Austin.—p. 373.
Psoriasis: Clinical and Laboratory Statistical Study. J. F. Madden, St. Paul.—p. 381.
Further Studies in Use of Quinidine in Treatment of Cardiac Irregularities. S. A. Weisman, Minneapolis.—p. 385.
Powers and Duties of Township Boards of Health in Minnesota. O. C. Pierson, St. Paul.—p. 390.
Ultraviolet Therapy. M. E. Knapp, Minneapolis.—p. 394.
Perforating Wounds. J. M. Culligan, St. Paul.—p. 397.
Noncommunicating Cyst of Septum Pellucidum, with Recovery Following Ventriculography. N. J. Berkwitz, Minneapolis.—p. 402.

Sulfanilamide and Specific Serum for Pneumococcic Meningitis.—Gray and Adams report a bacteriologically proved case of pneumococcic meningitis with recovery. The condition was complicated by granulocytopenia and otitis media and had the unusual residual of complete involvement of both bilateral eighth cranial nerves. Both sulfanilamide and specific serum were used and therefore the efficacy of either one alone could not be determined. Spinal drainages were done daily just preceding each intraspinal injection of serum and for four days after serum was discontinued. The drainages were probably a helpful therapeutic adjunct but no more than that. Eradicating a focus of pneumococcic infection, had there been one present, would have been of more value. The total amount of serum given was about twice that which is now considered sufficient. The granulocytopenia was due to toxicity or idiosyncrasy to sulfanilamide, since the patient had nausea and vomiting when the blood level of the drug was only 5.3 mg. per hundred cubic centimeters and had a secondary rise in temperature four days before the leukocyte changes were noticed. Although the patient was catheterized twenty-five times the urine was regularly negative, probably because of the antiseptic action of the sulfanilamide.

New England Journal of Medicine, Boston

220: 901-942 (June 1) 1939

Augustin Belloste and Treatment for Avulsion of Scalp: The Odd History of an Operation in Head Surgery. L. M. Strayer, Stratford, Conn.—p. 901.
Chemical Structure: Biologic Action: Therapeutic Effect. S. Weiss, Boston.—p. 906.
*Treatment of Tetany with Dihydrotachysterol (A. T. 10). L. M. Hurxthal, Boston, and T. S. Claiborne, Atlanta, Ga.—p. 911.
*Treatment of Severe Carbuncles by X-Ray. F. W. O'Brien, Boston.—p. 917.
Urology. W. C. Quinby, Boston.—p. 920.

220: 943-978 (June 8) 1939

The Heart in Anemia. L. B. Ellis and J. M. Faulkner, Boston.—p. 943.
Delirium Tremens: Study of Cases at the Boston City Hospital, 1915 to 1936. M. Moore and M. Geneva Gray, Boston.—p. 953.
Transmission of Encephalomyelitis in the Horse and Possible Vectors in the Human Being. J. S. Simmons, Boston.—p. 956.
Tuberculosis. D. S. King, Brookline, Mass.—p. 959.

Dihydrotachysterol for Tetany.—Hurxthal and Claiborne used dihydrotachysterol in six cases of postoperative tetany. The status of these patients was well known, as they had had tetany for two years or more. Four could be symptomatically controlled with calcium by mouth. Only three patients are still taking the preparation; the others had to discontinue its use because of its high cost. In the milder cases, calcium by mouth was stopped for from two to four weeks; dihydrotachysterol was then begun in doses ranging from 12 to 20 cc. during the first four or five days, but thereafter it was reduced to 1 cc. daily or 1 cc. every other day. In the severe cases calcium was stopped and the preparation was begun immediately in larger doses, but shortly thereafter from 1 to 3 cc. daily was prescribed. Later, available calcium in the form of calcium lactate, chloride or gluconate was prescribed orally. No toxic symptoms were observed except in cases in which the blood calcium rose above normal. Two patients had a hypercalcemia. In one of these, headache developed and the patient had an extreme aversion to taking the calcium; nausea was also present. The other patient complained of loss of appetite, nausea, headache and lassitude. Both patients soon lost their symptoms when the preparation was discontinued; one even went through pregnancy without additional medication. Following delivery the dose was increased, during which time hypercalcemia developed. The daily requirement of the preparation apparently depends on the extent of the deficiency. Doses of from 2 to 5 cc. weekly are sufficient to control the milder moderate cases. When the blood calcium has reached a normal level, an arbitrary dose of from 0.5 to 2 cc. is prescribed until the daily or weekly requirement is worked out. It is advisable to give calcium by mouth whenever it can be tolerated, as it reduces the amount of the preparation required and in turn provides soluble calcium. In spite of arguments in favor of other calcium preparations, calcium lactate in the authors' experience is most tolerable.

Roentgen Treatment of Carbuncles.—O'Brien points out that the mortality among 130 hospitalized patients with severe carbuncle receiving roentgen therapy alone or in conjunction with surgery was 3 per cent. There were no deaths among fifty-seven patients with facial carbuncle treated either alone

or chiefly by radiation. There was no evidence that carbuncle in the diabetic patient was a contraindication to roentgen therapy. The sixty patients who were treated early only by x-rays had a shorter convalescence than did the others.

Oklahoma State Medical Assn. Journal, McAlester

32: 191-246 (June) 1939

Septicemia. G. A. LaMotte, Oklahoma City.—p. 191.
Remarks on Treatment of Dacryocystitis. D. L. Edwards, Tulsa.—p. 199.
Diverticulum of Bladder. J. H. Howe, Ponca City.—p. 201.
A Bug Full of Tricks. L. J. Moorman, Oklahoma City.—p. 204.
Perforation of Hollow Viscus: Roentgen Aspects. E. D. Greenberger, McAlester.—p. 210.
Perinephric Abscess. C. M. O'Leary and R. Belend, Oklahoma City.—p. 214.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

47: 297-356 (June) 1939

Injection of Air for Localization of Lesions in Spinal Canal—Pneumomyelography. F. L. Reichert, San Francisco.—p. 297.
*Testosterone Propionate in Treatment of Gynecologic Disorders: Preliminary Report. J. P. Greenhill and S. C. Freed, Chicago.—p. 301.
Water Exchange in Relation to Toxemias of Pregnancy. F. L. McPhail, Great Falls, Mont.—p. 306.
Effect of Destruction of Germinal Crescent on Origin of Germ Cells and Development of Gonads in the Domestic Fowl. J. M. Essenberg and A. J. Svejda, Chicago.—p. 318.
Isotopic Metallic Iodine in Treatment of Syphilis. P. C. Barrette and K. M. McCoy, San Jose, Calif.—p. 328.
Tetany in Preeclamptic Toxemia. J. C. Brougher, Vancouver, Wash.—p. 331.
Organotherapy. B. Vidgoff, Portland, Ore.—p. 334.
Surgical Approach to Hypertension: Division VI. F. M. Findlay, San Diego, Calif.—p. 339.

Testosterone Propionate for Gynecologic Disorders.—In the treatment of twenty-two patients with various functional gynecologic disorders Greenhill and Freed used testosterone propionate. The patients were placed in three groups, those receiving injections during the first two weeks of the menstrual period, the second two weeks and the entire month. The doses of testosterone propionate ranged from 25 to 50 mg. every other day except on a few occasions when even more was administered. Injections of from 25 to 50 mg. every other day during the first two weeks relieved only two of the eight patients, one with menorrhagia and one with dysmenorrhea and menorrhagia. The improvement was judged to be about 50 per cent. One patient with dysmenorrhea and menorrhagia received 850 mg. during this period without relief. The menses in this case were, however, delayed for about twenty days. Injections of from 25 to 50 mg. to four patients with dysmenorrhea and two with premenstrual tension during the second two weeks of the period produced complete relief in one case of dysmenorrhea, moderate relief in two and slight relief in one. The two patients with premenstrual tension were not improved. The menses of patients in this group were not delayed significantly. The third group made up the most distressing cases: four patients with severe functional menorrhagia, two with excessive bleeding due to fibroids, one of dysmenorrhea and one with premenstrual migraine. The amount injected in all except the case of premenstrual migraine was 500 mg. or more during the month; the patient with migraine received 250 mg. during this time. The results in this group were gratifying in that one patient with severe functional dysmenorrhea improved considerably and one patient with intractable menorrhagia and dysmenorrhea who received 800 mg. in one month had normal periods for the first time in many years despite extensive endocrine therapy of all sorts. One patient with menorrhagia failed to improve and required irradiation of the ovaries. The two patients with bleeding due to fibroids responded very well. During the period of injections the fibroids regressed but within two months after the injections were stopped they returned to normal size, although the excessive bleeding did not reappear. Two patients with functional menorrhagia had an associated endometrial hyperplasia of the "Swiss cheese" type. The endometrium in both cases underwent atrophy and the bleeding ceased for at least two months. The patient with migraine was unimproved. Menses were suppressed in all patients in this group who responded well to this therapy.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Anaesthesia, Manchester

16: 81-124 (April) 1939

Blood Supply Changes During Cyclopropane Anesthesia. W. Neff, J. A. Stiles and R. Michelson.—p. 83.
Association of Atropine with Ether Convulsions. H. G. Dodd.—p. 90.
Deaths Under Anesthesia from 1921 to the Present Date. R. Jarman.—p. 100.

British Journal of Surgery, Bristol

26: 661-980 (April) 1939

Tuberculosis of Spleen with Tuberculous Subphrenic Abscess. W. G. Gill and W. N. Mann.—p. 661.
Adolescent Deformities of Acetabulum: Investigation into Nature of Protrusio Acetabuli. J. Gilmour.—p. 670.
Relationship of Acetabular Deformity to Spontaneous Osteo-Arthritis of Hip Joint: Investigation of Intra-Articular Factors Which Predispose to Osteo-Arthritic Degeneration. J. Gilmour.—p. 700.
Osteitis Fibrosa Disseminata: Report of Case. M. Coleman.—p. 705.
Complete Thyroglossal Fistulas. V. J. Kinsella.—p. 714.
Closed Operation for Intracapsular Fracture of Neck of Femur: Final Results in Recent and Old Cases. T. King.—p. 721.
Problems of "Black Out" in Aviation (Amaurosis Fugax). P. C. Livingston.—p. 749.
Carcinoma of Lower End of Common Bile Duct. J. C. Dick.—p. 757.
Operative Treatment of Stenosis of Vesical Neck. W. K. Irwin.—p. 764.
Observations on Simple and Malignant Pathologic Conditions of Breast. Thirza Redman and J. T. Hewetson.—p. 768.
Massive Necrosis of Muscles of Leg After Operation for Removal of Bone Graft from Tibia. N. R. Smith.—p. 780.
Detachment of Medial Epicondyle of Humerus with Displacement into Elbow Joint. E. J. R. Smith.—p. 785.
Congenital Dislocation of Hip. B. McFarland.—p. 791.
Chronic Nontuberculous Disease of Epididymis. D. McGavin.—p. 800.
*Pituitary Adenomas: Follow-Up Study of Surgical Results in 338 Cases (Dr. Harvey Cushing's Series). W. R. Henderson.—p. 811.
Surgery of Adrenal Cortex. L. R. Broster.—p. 925.

Pituitary Adenomas.—Henderson reports the surgical results of 338 histologically verified pituitary tumors observed at the Brigham Hospital during a period of twenty years. The report deals principally with surgical mortality statistics, the early results of operation and a follow-up study of the patients, the last of whom was operated on July 23, 1932. Only three of the 338 patients have not been heard from since their discharge from the hospital. There were 260 chromophobe adenomas (including thirty-two mixed adenomas), sixty-seven acidophil adenomas and eleven adenocarcinomas. No example of a basophil adenoma has been identified. The incidence of pituitary adenomas in Cushing's series of 2,023 verified intracranial tumors is 17.8 per cent. Chromophobe adenomas produce only local compression effects, whereas acidophil adenomas evoke general constitutional disturbances and often local effects in addition. The adenocarcinomas are apt to infiltrate surrounding structures. The various extrasellar extensions are surgically important. The operative procedures are referred to briefly, especially the more radical excavation of the intrasellar tumor and the immediate liberation of the chiasma by the transfrontal operation; also the importance of ventriculography in selected cases with intracranial extensions and the use of lateral flaps for the removal of extensions which are shown by ventriculography to be accessible. The late results, analyzed on the basis of the duration of improvement after operation, indicate great variability in the rate of growth and behavior of the chromophobe adenomas. After a successful transsphenoidal operation without irradiation some patients had no further trouble for as long as twenty years. On the other hand, a rapid recurrence within two or three years may take place even after a far more radical transfrontal operation plus roentgen treatment. While many patients maintained this improved status for from ten to twenty years, 95 per cent of those who had a recurrence showed indications of it within five years after operation. The clinical course of acidophil adenomas differs from that of the chromophobe adenomas. The two types of symptoms—local pressure (visual) effects and systemic effects—frequently show spontaneous remissions and exacerbations and often respond differently to treatment. Operation usually produces marked improvement in vision but may have no effect on the severe headaches, especially in cases in which there is a small tumor. The systemic disturbances are

ultimately apt to be the most serious because of the deleterious effects of the hormone secretion on the cardiovascular system and on sugar metabolism. The operative mortality is slightly higher than for the chromophobe adenomas, but the late surgical results appear to be better. The acidophil tumors are more amenable to roentgen therapy. The adenocarcinomas have not yet been subjected to sufficiently thorough pathologic study. Clinically, some of them behave like chromophobe adenomas; others, however, are hopelessly malignant, infiltrate the base of the skull and produce multiple cranial nerve palsies.

British Medical Journal, London

1: 963-1014 (May 13) 1939

Industrial Incapacity and Modern Medicine. D. Stewart.—p. 963.
Foreign Bodies. I. Fraser.—p. 967.
Effect of Desoxycorticosterone Acetate and Cortin on Salt Elimination in Addison's Disease. H. W. Dryerre.—p. 971.
*Progesterone and the Nasal Mucosa. J. K. Willson-Pepper and H. Royle.—p. 974.
Psychiatric Syndromes in Myasthenia Gravis. R. T. Collins.—p. 975.
Recent Work on Quality of Heat Rays. L. Hill.—p. 977.

Progesterone and the Nasal Mucosa.—Willson-Pepper and Royle report a case in which menorrhagia had existed for two years and spasmodic rhinorrhea of considerable severity for eighteen months. The nasal passages had been examined thoroughly and roentgenograms of the nasal sinuses were made but no evidence of infection had been found. The nasal septum was removed, as it was partially blocking the airway, but this failed to give relief. After the first injection of progesterone the nasal discharge and congestion immediately subsided and has not reappeared for several weeks. That some relationship may exist between the nasal mucosa and sexual activity has been observed for centuries. The effect of progesterone, the authors believe, in controlling severe rhinorrhea merits further investigation and if carried out in a sufficient number of suitable cases might yield valuable results.

Edinburgh Medical Journal

46: 305-368 (May) 1939

Hepatitis. J. W. McNee.—p. 305.
Psychotherapy in General Practice. T. A. Ross.—p. 313.
Carcinoma of Head of Pancreas: Case Treated by Radical Operation. C. F. W. Illingworth.—p. 331.
Observations on Virus of Influenza, with View to Elaborating a Simple Diagnostic Test Whereby Its Presence in Respiratory Tract of Man May Be Revealed. W. J. Tulloch.—p. 340.

International Journal of Psycho-Analysis, London

20: 137-222 (April) 1939

Retaining Sense of Reality in States of Depersonalization. C. P. Oberndorf.—p. 137.
Criteria for Interpretation. Susan Isaacs.—p. 148.
Some Observations on Ego Development of the Fetishist. S. M. Payne.—p. 161.
Role of Female Penis Phantasy in Male Character Formation. S. Lorand.—p. 171.

Lancet, London

1: 1083-1138 (May 13) 1939

Clinical Sense and Clinical Science. J. A. Ryle.—p. 1083.
*Control of Staphylococcus Aureus in an Operating Theater. E. A. Devenish and A. A. Miles.—p. 1088.
Abdominal Resection for Rectal Cancer. E. G. Muir.—p. 1094.
*Specific Gravity of Blood in Pneumonia. J. J. Elphinstone and E. M. Ward.—p. 1097.
Pneumococcic Meningitis: Report on Five Consecutive Cases Treated with Sulfanilamide-Pyridine (M. & B. 693). R. C. MacKeith and G. Oppenheimer.—p. 1099.
Fatal Case of Pneumococcic Meningitis Treated with Sulfapyridine. K. May.—p. 1100.
Pneumococcic Meningitis Treated with Sulfapyridine. P. S. Raman.—p. 1101.
Displaced Ribs. W. A. Ball.—p. 1102.

Control of Staphylococci in Operating Room.—Devenish and Miles encountered a high incidence of suppuration due to Staphylococcus aureus in "clean" operative wounds which was due to the leakage of Staphylococcus aureus through glove punctures from the skin of one surgeon who proved to be a skin carrier. The Staphylococcus aureus present in the air of the operating room and on the skin of the patients operated on apparently played no part in the incidence of suppuration. Nasal carriers of Staphylococcus aureus among the operating staff do not constitute a danger, provided masks are made impermeable to direct droplet discharge from the nose and mouth. All the strains of Staphylococcus aureus tested on press plates fermented mannitol and produced a coagulase for human plasma. Skin carriers, negative by the ordinary swabbing tests, may sometimes be detected by cultivating the sweat from the inside of rubber gloves at the end of an operation. This method has the advantage of excluding positive results due to temporary superficial contamination of the skin. The frequency of glove puncture during operation was found to be as high as 24 per cent; this was reduced to 14 per cent by precautions to avoid puncture.

Specific Gravity of Blood in Pneumonia.—Elphinstone and Ward determined daily the specific gravity of the blood in fifty-four consecutive cases of acute lobar pneumonia (forty-two men and twelve women). Leake, Kohl and Stebbins report an average figure of 1.0568. The specific gravity of the blood is said to be three or four degrees lower in women than in men. It is more constant in normal or convalescent subjects from day to day than in patients with pneumonia. Since fewer estimations of the specific gravity of the blood were possible in some cases than in others, the highest figure recorded for each patient is regarded as the most satisfactory common denominator. Consideration of the highest figure for each patient in relation to the severity of the illness shows that the specific gravity of the blood was above 1.059 in only four of the thirty-two mild and average cases, whereas figures above 1.059 were recorded in fifteen of the twenty-two severe and fatal cases. Among the fatal cases the highest recorded specific gravity of the blood was below 1.06 almost as often as not. Of the fourteen patients whose highest figure was from 1.06 to 1.062 only four died, but nine were seriously ill. Of the six patients with figures of 1.063 or more five died, a mortality of over 80 per cent compared with 30 per cent for the whole series, and less than 25 per cent for the patients with a specific gravity of the blood of below 1.063. Thus the severity of the illness was apparently related to the specific gravity of the blood.

Medical Journal of Australia, Sydney

1: 637-674 (April 29) 1939

Herpes Simplex: New Point of View. F. M. Burnet and S. W. Williams.—p. 637.
Nonvenereal Infections of Genito-Urinary Organs. M. G. Sutton.—p. 642.

1: 673-712 (May 6) 1939

"To Guard Is Better Than to Heal." A. Webb-Johnson.—p. 673.
*Clinical Application of Thyrotrophic Hormone. K. S. Harrison.—p. 681.
Sulfonamide Chemotherapy in Gonorrhea. N. M. Gibson and C. J. Wiley.—p. 686.
Further Observations on Endemic Typhus in New Guinea. C. E. M. Gunther and A. G. Schroeder.—p. 688.
Comparative Anatomy of Knee Joint in Relation to Congenital Anomalies. S. Scougall.—p. 691.

Thyrotrophic Hormone.—Harrison gave thyrotrophic hormone to five patients exhibiting different types of thyroid insufficiency. The patients were all maintained at rest in bed for some time before and during the period of study. The basal metabolism estimations were performed by the Douglas bag technic. Two patients with secondary thyroid insufficiency showed an elevation of the basal metabolic rate following the administration of the hormone, two with primary hypothyroidism responded slightly and a patient whose thyroid had been removed gave no response at all. In four of the five patients the administration of hormone was followed by a significant fall in blood cholesterol. The fall in the blood cholesterol level might have been effected by the stimulation of a residuum of thyroid tissue which was not sufficiently large to elevate the basal metabolic rate. In other words, the cholesterol level of the blood might have responded more sensitively than the metabolic rate to a slight increase of thyroid activity. Those conditions which should provide the only fertile field for prolonged therapy with thyrotrophic hormone are those in which there is secondary hypothyroidism due to a primary pituitary insufficiency. Some such patients respond to thyroid extract less rapidly than do patients suffering from a similar degree of primary thyroid insufficiency. A test dose of thyrotrophic hormone will help to distinguish between primary thyroid insufficiency and hypothyroidism secondary to pituitary insufficiency.

Archives des Maladies du Cœur, Paris

33: 449-544 (May) 1939

Value of Auriculoventricular Dissociations in Diagnosis of Congenital Malformations of Heart. C. Laubry, P. Soulié and P. Marre.—p. 449.
Slow Malignant Streptococcicosis Grafted on Permeable Arterial Canal After Dental Avulsion: Dental Origin of Malignant Endocarditis. J. Fleury.—p. 464.
Evaluation of Renal Factor in Patients with Heart Disease by Determination of Coefficient of van Slyke. J. F. Porge.—p. 469.
*Evolution of Varices in Course of Pregnancy. H. Vignes.—p. 478.
Method of Individual Evaluation of Electrocardiograms. P. Benedetti. —p. 491.
Lian-Minot Electrocardiograph with Double Explorator, One by Contact, the Other Luminous and Acting at a Distance. C. Lian and G. Minot.—p. 497.
Cirsoid Aneurysm of Forehead: Phonocardiographic Particularities of This Lesion. H. Bonan and A. Calo.—p. 506.

Varices in Course of Pregnancy.—Vignes studied 131 pregnant women, of whom seventy-six were primiparas and fifty-five were multiparas; forty-one of the primiparas and twenty-three of the multiparas were without varices; nine of the primiparas and four of the multiparas had had varices before gestation. Of the fifty-four women who had gravidic varices, twenty-six were primiparas and twenty-eight multiparas. Pregnancy is the time at which varices are most likely to appear. In this connection the author cites Stubel, who reported that of fifty-four women with varices forty-eight attributed the onset of the disorder to a pregnancy. The time of appearance of gravidic varices differs. In some women their appearance is a veritable diagnostic sign of pregnancy in that they appear shortly after the first suppressed menstruation. Of thirty-one women of the author's material in whom the time of appearance of the varices was known, twelve developed the varices during the first three months of pregnancy, fifteen during the second three months period and four during the seventh month. He concludes from this that in the majority of cases the varices appear before the volume of the uterus can hinder the course of blood in the legs. The varices are most frequently located in the legs. However, other localizations are possible: they have been observed on the arms but especially on the vulva, vagina, uterus, round ligaments, suprapubic region and breasts. The varices of the round ligament may give rise to an incorrect diagnosis in that they are readily mistaken for inguinal hernia. The varices appearing in the course of a pregnancy generally undergo involution which may even lead to complete disappearance. This possibility of their amelioration contraindicates treatments disproportionate with their benign character. Discussing the causes of gravidic varices, the author shows that the imperfection of the mechanical explanations leads to emphasis on the role assumed by insufficiency of the venous tonus, which in turn may be due to various factors (constitutional, hereditary endocrine and so on). In the last part of his discussion he calls attention to the fact that during as well as outside of pregnancy varices may lead to diverse complications such as rupture, eczema, ulcer, neuritis, phlebitis and periphlebitis. Rupture is noteworthy when it occurs in the region of the vagina or of the uterine cervix, since the resulting hemorrhages may be taken for a symptom of placenta praevia. If varices are ruptured in the region of the parametrium they may give rise to large hematomas, which in turn may cause dystocia. The author directs attention to varicose phlebitis and periphlebitis, although he admits that they are not frequent. Periphlebitis may lead to obliteration of the vein and terminate in suppuration; varicose phlebitis may give rise to fatal pulmonary embolism.

Journal de Médecine de Lyon, Lyons

20: 351-380 (June 5) 1939

Autochthonous Kala-Azar in Child Aged 11. M. Bernheim and P. Sedallian.—p. 351.
Auto-Agglutination of Erythrocytes (Observed in Case of Kala-Azar). P. Sedallian and P. Monnet.—p. 361.
*Osteopathies Caused by Bismuth. J. Racouchot.—p. 367.
*Reactions of Cerebrospinal Fluid in Course of Chronic Polyarthritis. J. Graber-Duvernay and F. Gerbay.—p. 371.

Osteopathies Caused by Bismuth.—Racouchot demonstrates that the abuse of the therapeutic application of metals, especially bismuth, gives rise to osteopathies. They are, in general, of the osteoporotic type. The author cites several case histories and shows that the osseous resorption of bismuth is of the same type as that which is encountered in cases of lead poisoning. In this connection he cites observations and experiments made by Askanazy and Rutishauser. These investigators observed osseous changes in lead poisoning and were able to produce osteopathies experimentally, demonstrating that metals are of primary importance among the exogenic causes of osteopathy. The author suggests the term osteopathy because in the absence of anatomic verification it is impossible to determine the exact nature of the osseous process. He says that the relation between the metal and the osseous disorder is not surprising if attention is given to certain conditions that are observed in the course of bismuth therapy. He cites the osteo-articular pains; the phosphaturia, which is indicative of considerable decalcification; the frequency of gluteal calcifications at the point of injection of bismuth, and finally the buccal elimination of bismuth. Like lead and mercury, bismuth is eliminated with predilection at the gums. The author says that although the osteopathies caused by bismuth are comparatively rare, there is danger that they may increase if bismuth is administered over long periods.

Cerebrospinal Fluid in Chronic Polyarthritis.—Graber-Duvernay and Gerbay studied the cerebrospinal fluid in chronic polyarthritis with regard to the formulation of the prognosis, the selection of the treatment, particularly of chemotherapy, in the differentiation of the chronic forms and in similar problems. Their clinical material was comparatively limited; that is, they made their investigations on eighteen patients with chronic polyarthritis. Although they were unable to obtain definite answers to all the questions, they found that there is usually an augmentation of the albumin content of the cerebrospinal fluid in chronic polyarthritis; however, the sugar content does not undergo variations and the cell count likewise reveals normal values. The authors raise the question whether this dissociation between the albumin content and the cell count is the manifestation of a meningomedullary compression or at least of a more or less discrete arachnoidoradicular one. They point out that ordinarily the presence of hyperalbuminosis indicates a lesion of the nervous system and they cite observations which indicate a nervous involvement in chronic polyarthritis. They found that the hyperalbuminosis is an extremely early sign and is of prognostic and diagnostic significance. A lumbar puncture is indicated when doubts exist about the evolutive character of a polyarthritis; if it reveals the presence of a hyperalbuminosis, the prognosis must be made with reservation and active treatment, such as gold therapy, is indicated. The examination of the cerebrospinal fluid seems to be superior to that of the sedimentation speed of the erythrocytes in determining the advisability of the resumption of chemotherapy. In cases of chronic polyarthritis with moderately accelerated sedimentation speed a new series of treatments with gold salts is unnecessary if the albumin content of the cerebrospinal fluid is normal. The exploration of the subarachnoid space has an important part also in determining the advisability of articular redressements, because the clinical aspects frequently do not give sufficient information in this respect. The authors show that it is inadvisable to resort to articular redressement whenever there exists a hyperalbuminosis of the cerebrospinal fluid; that is, whenever the albumin content exceeds 0.5 Gm.

Journal d'Urologie Médicale et Chirurgicale, Paris

47: 369-464 (May) 1939

Anterior Perinephric Phlegmon. Vergoz and Lenck.—p. 369.
*Treatment of Prostatic Retention of Urine by Endo-Urethral Resection of Prostate. R. Denis.—p. 395.
Endo-Urethral Treatment of Retention of Urine Caused by Cancer of Prostate. R. Denis and P. Dufour.—p. 410.

Endo-Urethral Resection of Prostate.—Denis presents his report on endo-urethral resections for prostatic hypertrophy and says that since 1934 he has treated all operable prostatic retentions by the urethral route, no matter what was the volume of the prostate or the age of the patient; he thought that by thus extending the indications for endo-urethral resection to the limit it would be possible to obtain an insight into the real value of the method and then the indications could be limited on the basis of the disappointments. The author operated on

105 patients "with closed bladder." For 103 of these patients the results were favorable, one patient died and for another one the operation was a failure, it having resulted in a definite cystotomy. The operation was performed also on thirty-five patients "with open bladder." Among this group there were two deaths and two failures; in the other thirty-one patients normal micturition was restored. The author analyzes his observations on the two groups of cases and says that endo-urethral resection is easy in the small prostatic hypertrophies but rather difficult in hypertrophies of considerable volume. He thinks that this explains why the majority of surgeons limit this operation to the small prostates. However, it is important to know that the chief difficulty is encountered at the beginning of the resection, that is, after the beak of the apparatus has hardly passed the obstacle; it is not mobile, the field is extremely narrow and the introduction of the apparatus has already caused so much bleeding that the surgeon is much inconvenienced by the hemorrhage. At this point the resection should not be given up, because after several rapid cuts of the knife the apparatus is mobilized, hemostasis is made and the field is enlarged; after several more cuts the hemorrhage is arrested with great care and there is sufficient space so that the volume of the organ is no longer a hindrance and the surgeon is master of the situation. The resection is then carried out methodically, each lobe in its turn. The difficulty now is in determining the moment when it is necessary to stop because the resection is sufficient. The author discusses the procedure on the median and lateral lobes. In the conclusion he stresses that he is glad that he introduced endo-urethral resection into his current urologic practice. He does not regret that he employed the method even on large prostates. The majority of patients have clear urine, no difficulty of micturition and no residue. The author observed no relapses and the patients were satisfied.

Sang, Paris

13: 467-578 (No. 5) 1939

*Benzene Myelotoxicosis: Clinical and Hematologic Study of Ten Cases of Occupational Intoxication by Benzene Compounds. M. Lamy, P. Kissel and L. Pierquin.—p. 467.
Anemia of Acute Malaria. J. Lebon and A. Manceaux.—p. 489.
Grave Acute Hemolytic Anemia with Leukemoid Aspects, Following an Angina Treated by Various Chemical Agents: Pathogenic Considerations. N. Gingold and G. Comsa.—p. 517.

Benzene Myelotoxicosis.—Lamy and his associates studied most of their patients over periods lasting several months, the bone marrow was studied in all and in some of them repeatedly. Moreover, in four fatal cases they were able to compare the myelograms with the histologic pictures of the bone marrow. The studies were made on ten workers of a shoe factory who had been exposed to chronic intoxication by benzene compounds. The intoxications were severe, five of them resulting in death. The authors describe the histories of the ten patients and also give a tabular survey which lists the clinical signs, the hematologic and medullary aspects, the final outcome and the post-mortem observations on the bone marrow in the fatal cases. Further they discuss the variable evolution of benzene poisoning, the changes on organs other than the bone marrow, particularly the liver, the prognosis and the therapy. Summarizing their observations they state that in the majority of cases the benzene intoxication produces a complex hematologic syndrome which is characterized by the signs of anemia, purpura and granulocytopenia. In contradistinction to this uniform hematologic picture, the myelographic aspects are multiform: in the mild cases, there exists a simple erythroblastic reaction; in the grave cases there exists total medullary aplasia, perhaps associated with a hyperplasia of the cells of the reticulo-endothelial system. Reservation is necessary in estimating the prognosis of the benzene hemopathies, for even after the patients have been removed from intoxication they are still subject to relapses. Repeated examinations of the blood and of the bone marrow are indispensable for the establishment of the prognosis. The therapy of grave benzene hemopathies is extremely deceptive. Only repeated blood transfusions have any efficacy. The authors think that the only efficient prevention of occupational intoxication with benzene compounds consists in legal or administrative regulations prohibiting the use of benzene compounds in certain industries.

Helvetica Medica Acta, Basel

6: 147-288 (May) 1939

Birth Control. A. Labhardt.—p. 147.
Movement of Population and Birth Control. Koenig.—p. 185.
*Late Results of Surgical Sterilization of Women. R. Wenner.—p. 209.
Löffler's Eosinophil Pulmonary Infiltrate: Case. K. von Neergaard.—p. 224.
Pneumatosis Cystoides Intestini. M. Dresder.—p. 229.
Experimental Contribution to Treatment of Hypertension. F. Rothschild and C. Meili.—p. 255.
Contribution to Study of Surface Tension of Blood Serum. A. Gigon and M. Noverraz.—p. 264.

Late Results of Surgical Sterilization in Women.—In order to determine how women feel about sterilization in their later years, Wenner sent questionnaires to the women who had undergone sterilization at the clinic in Basel during the years between 1920 and 1933. A table which lists the indications for the 1,069 sterilizations shows that in 174 cases social factors were the only indications and that in 126 additional cases the social factors motivated the sterilizing operation, but there existed some other factor (medical, gynecologic or eugenic) which further supported the advisability of the sterilization. The author reproduces the questionnaire that was submitted to 904 of the 1,069 women and was answered by 742 of them. Of this number thirty-six, 4.8 per cent, were not satisfied and regretted the sterilization. Seven of these had physical complaints (pains, ovarian insufficiency and so on); in all others the complaints were of a psychic nature, such as unrequited maternal instinct, feeling of inferiority, mental depression, religious scruples and frigidity. From the fact that 95.2 per cent of the women were satisfied with the results of the sterilization, the author concludes that there is no need to deviate from the course that has been followed so far.

Monatsschrift für Geburtshülfe und Gynäkologie, Basel

109: 1-72 (April) 1939

*Early Diagnosis of Carcinoma of the Cervix Uteri. H. Wespi and D. Brasch.—p. 4.
Estrogen Excretions in Urine of Pregnant Women. Elisabeth Dingemanse, E. Laqueur and O. Mühlbock.—p. 37.
Syphilis and Carcinomas of the Cervix Uteri. M. Sorba.—p. 49.

Diagnosis of Carcinoma of Cervix.—Wespi and Brasch report the clinical observations in nine cases of primary carcinoma of the cervix. These observations extended over more than two years, the authors employing the colposcope, the iodine test and microscopic analyses on the basis of Hinselmann's classification. The age of the patients ranged between 32 and 52 years, with an average of 41.5. The authors' purpose was to arrive at a comparative evaluation of the microscopic and colposcopic pictures and a rapid survey of the extension and nature of histologic modifications. Serial sections were performed on eight patients. The nine patients were divided into three groups. In group 1 (five patients) carcinoma was discovered only through the colposcope. In group 2 (two patients) colposcopy confirmed macroscopic suspicions. In group 3 (two patients) one case of carcinoma was detected without the colposcope; in the other case the malady was too deep seated to admit of colposcopic determination. In their epicritical comments the authors point out several microscopic peculiarities. Besides areas with manifest inward penetration and pronounced atypias of a carcinomatous nature there were extensive portions with marked atypical epithelium but without any indication of penetrating growth, an indication of cancer of multicellular origin, the connection established by an atypical epithelium, called "matrix" by Hinselmann. In three patients abnormal epithelium was found besides the atypical. Nearly all of the seven patients successfully examined with the colposcope revealed various modifications such as leukoplakia, to which according to the authors no undue significance should be attached. Coarse, heavy proliferations and red surfaces that bled easily on being touched along with other "matrix" areas invited suspicion of the presence of a carcinoma. Whenever the atypical epithelium extended beyond the colposcopically suspected areas, application of the iodine test adjudicated the doubt. The authors state that they employed the Schiller test with greater frequency to distinguish patients with atypical and hence carcinomatous epithelium from those with abnormal epithelium. None of their patients showed the characteristic symptoms of early carcinoma, such as bleeding on contact and

bloody discharges. They therefore stress the significance of the period of latency and emphasize the value of precautionary examinations, if the colposcope and iodine test are resorted to from the beginning. In three of their cases the iodine test paved the way for subsequent colposcopy. In one case colposcopy had to be repeated a second time for the sake of diagnostic validity. The authors also note that surgical intervention frequently was attended by difficulties in technic because of periuterine inflammation. In all cases but one initial amputation had to be followed by complete excision, the latter resulting in one death.

Giornale Medico dell'Alto Adige, Bolzano

11: 125-180 (March) 1939. Partial Index

*Anemic Syndromes After Operations on Stomach. A. Chiatellino.—p. 125.
Consequences of Denervation of Thyroids. A. Chiatellino.—p. 146.

Anemic Syndromes After Gastric Operations.—Chiatellino examined the blood of 472 patients who had duodenal or peptic ulcer and who had undergone an operation on the stomach during the last few years. The operations consisted of resection (Reichel-Polya) in 224 cases, gastro-enterostomy in 197 and hemipylorectomy in fifty-one. The 200 men operated on (no matter what the type of operation) had a normal crasis of the blood. In eighteen of the thirty-one women who had gastric resection and in one of the twenty-six who had gastro-enterostomy, subacute hyperchromic anemia occurred which improved after administration of iron and recurred some time after its discontinuance. None of the eleven women who had hemipylorectomy developed anemia. Anemia did not develop in any of the cases sooner than two years after operation. The majority of the women who developed anemia were nearing the menopause. The author believes that operations on the stomach, especially resection, may induce a functional disorder for the assimilation of iron.

Arquivos de Cirurgia Clinica e Experimental, São Paulo

3: 1-95 (Feb.) 1939. Partial Index

*Surgical Treatment of Lymphogranulomatous Stenosing Rectitis. E. Vasconcelos.—p. 19.
Testicular Ectopia: Torek's Operation. N. M. Barros Filho.—p. 47.

Lymphogranulomatous Stenosing Rectitis.—Vasconcelos describes a technic for surgical treatment of lymphogranulomatous stenosing rectitis in women. In all cases the length of the sigmoidal segment and the evolutional phase of the disease are determined before the operation by x-ray examination and rectoscopy, respectively. When the sigmoid is long and there are no complications, the treatment consists in lowering the rectosigmoid segment toward the perineum, removing the involved portion of the rectum and suturing the sigmoid to the sphincter and perineum. If the segment is short and there are no complications and also when fistulas and sphincteral and genital lesions are already developed, the operation consists in making a permanent sigmoid anus and removing the involved segment including the rectal sphincter. The operation is made in two stages (abdominal and vaginoperineal). In all cases spinal anesthesia is used and salpingectomy is also performed. The steps of the abdominal stage include a median abdominal incision, exposure of the surgical field, sectioning of the pelvic peritoneum at the mesosigmoid, ligation of the local vessels, separation of the rectosigmoid segment from the neighboring structures down to the point at which the median hemorrhoidal vessels appear, pushing of the isolated colirectal segment toward the perineum, suturing of the cut pelvic peritoneum to the sigmoid after the latter is already lowered, and closure of the peritoneum by planes without the placing of any drain. The vaginoperineal steps include reconstruction of the ruptures of the perineum and of the rectal sphincter which were caused by the previous vaginorectotomy, further separation of the rectosigmoidal segment, ligation of the local vessels and removal of the involved segment through the perineum. The next technical details are rectoperineal reconstruction, myorraphia of the elevator muscles with sutures to the wall of the lowered colon, myorraphia of the sphincter, suture of the vaginal mucosa and of the anterior perineum and also suturing of the colon to the skin of the perineum. The draining or placing of a sound at the lumen of the intestine is not necessary, but a sound is temporarily left in the bladder. A permanent sigmoid anus is performed either with or without a previous vaginorectotomy by the technic described with the following modifications: The rectocolic segment is not pushed down to the perineum during the abdominal stage, but after it is isolated from the neighboring structures the sigmoid is cut. The proximal sigmoid segment is implanted to the abdominal wall at the iliac fossa for making a sigmoid anus, whereas the distal sigmoid-rectal segment is removed in a block together with the sphincter, the involved soft parts and the involved parts of the perineum, by the perineal route. Reconstruction of the elevator muscles, which are preserved, and suturing of the vagina and of the perineum are carried on by the ordinary technic.

Archiv für Kreislauforschung, Dresden

4: 189-392 (May) 1939

Electrocardiogram in Hyperfunction of Thyroid. K. Spang and C. Korth.—p. 189.
Investigations on Dynamics of Circulation Under Influence of Various Types of Baths. W. Herkel.—p. 313.
*Tendency to Normalization of Electrocardiogram of Patients with Angina Pectoris Undergoing Irradiation of Adrenals. W. Raab and E. Schönbrunner.—p. 362.

Electrocardiogram Following Irradiation of Adrenals.—According to Raab and Schönbrunner it has been suggested that in the so-called simple angina pectoris which appears during exertion, excitement, influence of cold and so on the excessive elimination of epinephrine from the adrenals is concerned in the causation. Since it has been demonstrated that roentgen irradiation of the adrenals restricts the production of epinephrine, it was decided to employ this treatment in angina pectoris. The authors describe electrocardiographic studies on thirty-eight patients with simple angina pectoris who were treated with roentgen irradiation of the adrenals. They found that twenty-eight of them were either improved or entirely free from symptoms after one or several series of roentgen irradiations. Sixteen of these twenty-eight improved patients had had a pathologic electrocardiogram before the treatment, that is, in thirteen the electrocardiogram had been of the type that is characteristic of diffuse or circumscribed hypoxemia of the myocardium and in three it had been of the type that is observed in disturbances of the intraventricular conduction. In ten of the thirteen patients who had had an electrocardiogram characteristic of hypoxemia the electrocardiogram, in harmony with the subjective condition, had become more or less completely normalized after the roentgen treatment. In the three other subjectively improved cases with the electrocardiographic aspects of hypoxemia and in three with those of irreversible intraventricular conduction disturbances there were no objective changes. One of the first three died four months later as the result of coronary occlusion. In seven patients with the electrocardiographic aspects of hypoxemia, in whom there was no subjective improvement following roentgen therapy, the roentgenogram likewise showed no tendency toward normalization. There were no relations between the height of the blood pressure and the reaction of the subjective condition and of the electrocardiogram. The frequent normalization of the electrocardiogram of patients with angina pectoris who were subjectively improved following roentgen irradiation of the adrenals objectively proves the efficacy of this treatment.

Klinische Wochenschrift, Berlin

18: 701-732 (May 20) 1939. Partial Index

Is Purine Metabolism Regulated by Hormones? F. Chrometzka.—p. 701.
Physiologic Significance of l-Ascorbic Acid Content (Vitamin C) in Human Tonsils and Relation of l-Ascorbic Acid to Defense Function of Tonsils. H. H. Meyer.—p. 704.
Behavior of Nontuberculous, Tuberculin-Sensitive Guinea Pigs Toward Intraperitoneal Injection of Tuberculin. G. Hensel.—p. 708.
Investigations on Disinfection of Hands in Surgery. F. Neufeld, O. Schiemann and H. Kuhn.—p. 710.
Modification of Glycogen Content of Liver by Ether Narcosis and Relation to Fat-Soluble Vitamins. H. J. Lauber and T. Bersin.—p. 715.
*Transfusion of Blood Conserved According to New Method. F. Corelli.—p. 716.
Attempt to Treat Case of Nontropical Sprue with Nicotinic Acid. H. Fuchs and A. Wisselinck.—p. 722.

Transfusion of Conserved Blood.—Corelli says that in the course of studies on allergic diseases he observed that if blood is brought together with various thiosulfate solutions it stays fluid and for many days, up to one month, it remains in

a good state of conservation. Recalling, moreover, that thiosulfate is not toxic and that it has a desensitizing effect, he decided to use it for the conservation of blood, the more so since blood transfusions may become complicated by allergic phenomena. One of the advantages of the use of thiosulfate is that a small quantity of solution is sufficient to keep the blood in a fluid state; other solutions that are used for this purpose, for instance the one employed by the Russians, requires equal amounts of blood and solution so that, if 400 cc. of blood is to be given, 800 cc. of fluid must be injected, which may not be always desirable. The author found that 7.5 cc. of solution of thiosulfate is sufficient to preserve 100 cc. of blood for more than one month. If blood is to be conserved only for a few hours, 7.5 cc. of thiosulfate solution is enough for from 125 to 150 cc. of blood. In the specimens of blood that were preserved with thiosulfate it was observed that, if the blood had been withdrawn from a fasting person, the supernatant fluid remained entirely clear. A slight hemolysis began at various times in some blood specimens between the tenth and fifteenth days, in others earlier or later. After numerous animal experiments had demonstrated that blood preserved by means of solution of thiosulfate is well tolerated, the author used this type of blood on human subjects. He used it in 450 transfusions in various internal, surgical and obstetric disorders. The quantities varied between 100 and 500 cc. and in some cases the transfusions were repeated. In the majority of cases the blood had been preserved for from one to two weeks, but some transfusions were made with blood that had been preserved for from sixty to sixty-two days. The technics of withdrawal and conservation as well as of transfusion are simple. If the conserved blood is to be used for transfusion it is merely heated in the water bath until it reaches a temperature of from 95 to 100.4 F. In order to insure homogenization the blood should be moved with rhythmic rotating movements while it is warming up. Transfusion is effected by simple intravenous injection. Temperature reactions occurred in only 8 per cent of the cases and they were usually slight. In order to avoid complications the author recommends that blood groups should be watched and that withdrawal as well as transfusion should be done while the persons are still fasting.

Zeitschrift für klinische Medizin, Berlin

136: 1-166 (April 21) 1939. Partial Index

Determination of Extracellular Water in Healthy Persons and Patients. Hermine Molenaar and D. Roller.—p. 1.

Comparative Clinical and Electrocardiographic Investigations on Diagnosis of Impairment of Right Side of Heart. F. Kienle.—p. 33.

Oxygen Provision of Organism. L. J. Del Baere.—p. 43.

Paratyphoid B, Dechloridation, Diffuse Glomerular Nephritis. K. Mellinghoff and H. Frigge.—p. 51.

*Recognition of Early Lesions of Plumbism with Aid of Observation of Cutaneous Capillaries During Life. H. Otto and G. Hahn.—p. 61.

Vitamin B_1 and Carbohydrate Metabolism. A. Wilson.—p. 77.

Change in Regulation of Blood Sugar Under Influence of Insulin with Delayed Action. R. Pannhorst and H. Bartelheimer.—p. 81.

Further Observations on Vascular Action of Sex Hormones. M. Ratschow and M. L. Steckner.—p. 140.

Early Lesions of Plumbism.—Otto and Hahn employed Müller's method of capillaroscopy for the detection of early lesions of plumbism. They report studies on fifty workers who for years had been soldering cables and who were not exposed to lead poisoning. Aside from some abnormalities of constitutional origin, the capillaroscopy disclosed no deviations from the normal. The simultaneous determination of the porphyrin content of the urine likewise revealed normal values in these persons. In fifty-five workers who sprayed varnish and who were exposed to lead poisoning, because many of the paints which they had to handle contained lead, the capillaroscopic aspects corresponded with the degree of exposure to lead poisoning. In 50 per cent of these workers there existed slightly atypical forms of the terminal loop with pathologic elongation coiling and winding; in 75 per cent more or less severe contractions of the arterial branch could be observed, and in almost 50 per cent of those with capillary contractions there existed a galloping current and in almost 30 per cent a more granular current. However, the examination of the urine for porphyrin gave better results for the estimation of the degree of lead intoxication in that the urinary elimination of porphyrin was increased in 80 per cent of the cases and in some cases the porphyrin values exceeded 500 micrograms. In two cases of severe plumbism, capillaroscopy disclosed ischemia in the field of observation in that the arterial branch of the capillaries was greatly contracted. The current was slightly to moderately granular. In these cases too the elimination of porphyrin was rather high. In six cases in which there had been severe lead poisoning, which had cleared up, capillaroscopy disclosed, outside of a few minor contractions and of coiling and the terminal loops, no signs of the former lead poisoning. The changes observed here could be explained on the basis of constitution and age. The porphyrin values of the urine were normal. In experiments on white rats it was found that injection of quantities of lead which were considerably below the lethal dose caused contraction of the capillaries with greater or lesser change in the current. On the basis of these results the authors reach the conclusion that the contractions, coilings and elongations observed in the capillaroscopy of patients exposed to lead intoxication are caused by spasms of the arterial branches of the capillaries. The anemia which develops in lead intoxication can be held responsible for some of the changes on the capillaries but not for all of them. Moreover, it may be assumed with some degree of probability that the capillary changes, which in the beginning are spastic and reversible, later become irreversible and give rise to the frequently observed arteriocapillary fibrosis. The authors stress further that these observations show again that the sensitivity toward lead and the severity of lead intoxication are largely due to the endogenically conditioned vasomotor instability. The majority of patients with lead intoxication belong to the group of persons with vasomotor instability. The authors reach the conclusion that, because of its greater clarity and simplicity, the quantitative determination of porphyrin in the urine is of greater diagnostic value in the early diagnosis of lead intoxication than is capillaroscopy. However, capillaroscopy may prove valuable as a complementary diagnostic procedure and it also provides information about the vascular pathology of lead intoxication.

Vrachebnoe Delo, Kharkov

21: 1-80 (No. 1) 1939. Partial Index

New Chemotherapeutic Methods in Bacterial Diseases. Ya. O. Gabel and F. L. Grinberg.—p. 5.

New Therapeutic Methods in Meningococcic Cerebrospinal Meningitis. A. A. Koltypin.—p. 9.

Further Observations on Antivirus of Mazur Therapy of Bone Tuberculosis. L. I. Shulutko.—p. 19.

Alterations in the Spleen and in the Lymph Nodes in Infectious Diseases. M. S. Milman.—p. 25.

Pathogenesis of Circulatory Disturbances in Shock. N. N. Gorev.—p. 31.

*Acute Abdominal Type of Hepatolenticular Degeneration. K. N. Tretyakov.—p. 37.

Insulin Lipodystrophy. L. I. Andres and A. I. Vilkomirskiy.—p. 45.

Hepatolenticular Degeneration.—Tretyakov reports a case in which a boy aged 12 was clinically diagnosed as having the acute abdominal type of hepatolenticular degeneration. The illness began with an acute febrile onset of obscure etiology, accompanied with manifestations of liver cirrhosis and portal stasis (splenomegaly, ascites and anasarca). These were followed by neurologic symptoms of spastic-convulsive lenticular type. The latter resembled tetanoid states but differed from tetany by the absence of mechanical or electrical nerve-muscle hyperirritability and by the presence of pyramidal symptoms pointing to lesions of the central nervous system. The combination of the neurologic symptoms of lenticular type with those of liver cirrhosis permitted the diagnosis of hepatolenticular degeneration.. Microscopic studies demonstrated characteristic sclerotic degeneration with an increased growth of cells of type 2 of Alzheimer and typical porous appearance of brain tissue. These alterations were found predominantly in the corpus striatum but were also present in the cerebral cortex, in the region of the aqueduct of Sylvius and in the cerebellar hemispheres. In the author's second case there was a febrile onset in a boy aged 10. Fifteen days later he developed right-sided hemiplegia with aphasia. In the next six weeks the sickness ran a course resembling that of septic endocarditis with an enlargement of the liver and the spleen, terminating in pneumonia. Three days before death the patient had convulsions of extensor-pronator type in both extremities and opisthotonos. Necropsy revealed a symmetrical subacute degeneration of the lenticular nuclei with formation of cavi-

ties and characteristic microscopic alterations as described by Wilson. The author regards this case as one of subacute lenticular degeneration closely resembling the abdominal type. Because hepatic symptoms in the author's first case preceded the cerebral symptoms by several months, the author feels that the liver lesion was the primary factor and the lesions of the nervous centers secondary. A further proof of the primary importance of the liver and metabolic disturbances is to be seen in the fact that the pathologic alterations of the nervous system are not systematic and are not only localized in the nucleus lentiformis but also involve the cerebral cortex, the substantia nigra, the nucleus dentatus of the cerebellum and the gray and the white matter without definite systematization.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

83: 2037-2204 (May 6) 1939. Partial Index

Difficulties in Diagnosis and Treatment of Malignant Laryngeal Tumors. A. de Kleyn.—p. 2040.
Investigations on New Gold Preparation Auron B. A. M. Ernst.—p. 2047.
Therapeutic Action of Auron B in Experimental Tuberculosis of Guinea Pigs. J. D. Verlinde.—p. 2054.
*Results of Modern Surgical Treatment of Ventricular (Duodenal) Ulcer. C. Knapper.—p. 2058.
Therapy of Trigeminal Neuralgia. E. Hoelen.—p. 2063.

Surgical Treatment of Ulcer.—Knapper reports the results of follow-up examinations on fifty patients who underwent surgical treatment for duodenal ulcer in the years between 1931 and 1937. All the patients had undergone one or several internal treatments before an operation was performed, the author being of the opinion that surgery should be resorted to only after the internal treatment of gastric ulcer has failed. In forty of his cases he performed gastric resection and in ten gastro-enterostomy. In case of duodenal ulcers and in those localized in the antrum pyloricum, he always performed the resection according to Polya, which is a modification of the second operation of Billroth. In ulcers high up on the small curvature he made use of Schoemaker's clamp, which makes possible the resection of a large portion of the small curvature (that containing the ulcer) without having to sacrifice the corresponding section of the large curvature. He completes this resection with a gastrointestinal anastomosis according to Polya, in contradistinction to Schoemaker, who employs the first operation of Billroth for this. Gastro-enterostomy was performed by Knapper always according to the same principle, namely in the form of a retrocolic posterior vertical gastro-jejunostomy. Four of the fifty patients (8 per cent) died as the result of the operation. Of those who survived, forty-four remained free from pain for from one to seven years after the operation and forty were entirely well. In one instance, gastro-enterostomy was without success. Since an interval of from one to seven years does not permit a definite evaluation of the surgical results, the author intends to repeat the follow-up examination after a few years.

Acta Medica Scandinavica, Stockholm

100: 1-158 (May 13) 1939

Myeloma with Spontaneously Crystallizing Protein in Blood Serum and Urine: Case. T. Packalen.—p. 1.
Electrocardiographic Investigations on Patients with Schizophrenia Undergoing Treatment with Metrazol. E. G. Regnér and B. Ewert.—p. 15.
*Medicoforensic Significance of Starvation. B. Stokvis and A. Naerebout.—p. 35.
Calcinosis Universalis. J. J. C. P. A. Roovers.—p. 57.
Consideration of Mechanical Factors in Blood Pressure. C. D. de Langen and J. G. ter Braak.—p. 72.
Attempts to Inhibit Growth of Jensen Tumors in Rats by Depot Treatment with Heparin. P. Hedenius.—p. 130.
Electrocardiogram in Auricular Infarct. R. Langendorf.—p. 136.
Reactions of Cerebrospinal Fluid in Course of Chronic Polyarthritis. J. Graber-Duvernay and F. Gerbay.—p. 150.

Medicoforensic Significance of Starvation.—Stokvis and Naerebout report the case history of a man who was on trial for attempted manslaughter and brutal maltreatment, which he had committed after he had been without food for about a day. The accused did not recall having committed the criminal acts, and investigations revealed that the brutalities represented the release of accumulated feelings of resentment on a day on which the accused had been without food, on which he had suffered from severe headaches and on which he had been unjustifiedly accused and deliberately made jealous by his fiancée. In connection with this case it was suggested that it is entirely possible that an amnesia exists for acts that have been committed at the time of reduced consciousness and that prolonged fasting results in abnormally low blood sugar values, which in turn create a predisposition for a reducion in consciousness. The authors decided to investigate the possible influence of the reduction of the blood sugar content following prolonged fasting on the state of consciousness. Following a review of the literature on experimental investigations regarding the influence of hunger on the psychic behavior, they describe their own studies on ten healthy persons. 1. They found that hunger is generally followed by a reduction in the sugar content of the blood. 2. Hunger causes a reduction in and instability of the state of consciousness. 3. There exists a certain connection between the reduction in the blood sugar content and the reduction in consciousness. 4. The general reduction of the degree of consciousness as well as the submersion of the consciousness, which occur in healthy persons during a period of starvation, must be taken into consideration in the psychiatric evaluation of delinquents who have committed criminal acts during hunger, regarding which amnesia may or may not exist.

Acta Radiologica, Stockholm

20: 105-212 (April 29) 1939

Malignant Tumors of the Skeletal Muscles, Fasciae, Joint Capsules, Tendon Sheaths and Bursae. G. Jönsson.—p. 105.
*Conservative Treatment, with Barium Enema, of Intussusception in Children. J. M. Nordentoft.—p. 128.
Simple Method for Stereometric Measurement. H. Christensen.—p. 137.
Combination of Sinusitis and Nonspecific Inflammatory Pulmonary Disorders. S. R. Kjellberg.—p. 147.
Widespread Subcutaneous Calcifications in Connective Tissue of Leg. G. Moberg.—p. 150.
Experimental Investigations on Significance of Protraction and Fractionation. B. Faber.—p. 170.
Radium Treatment of Cutaneous Cavernous Hemangiomas, Using Surface Application of Radium Tubes in Glass Capsules. M. Strandqvist.—p. 185.

Barium Sulfate Enema in Intussusception of Children.—After pointing out that the reduction of intussusception in children by means of a barium sulfate enema had been suggested as early as 1918 by Langley Porter of San Francisco and that it had been made use of in several countries since 1927, Nordentoft reviews a material comprising 440 cases of intussusception that occurred in Denmark during the years from 1928 to 1935. This survey reveals the increasing use of the barium enema for the examination and treatment of intussusception in children. During the latter half of this period about 33 per cent of all the cases were reduced by barium alone, of the roentgenologically examined about half. The author believes that nearly all forms of intussusception of the large intestine (colic and ileocecal) can be reduced in this manner if they come under treatment within the first twenty-four hours, and provided the attempt is done deliberately and energetically, with the use of an obturating rectal cannula and a constant high pressure. He stresses the importance of the picture of the evacuation and of repeated injection immediately after the fluoroscopic examination. Finally, he discusses briefly the advantages and drawbacks of the roentgenologic method.

Ugeskrift for Læger, Copenhagen

101: 593-622 (May 18) 1939

Frequency of Recurrence After Pneumothorax Treatment of Cavernous Pulmonary Tuberculosis. S. Cold.—p. 593.
*Percutaneous Tuberculin Plaster Test According to Monrad. A. Grut.—p. 597.
Movable Support for Neck for Use in Endoscopic Interventions. S. F. Nielsen.—p. 598.
Bandl's Ring—Amyl Nitrite. E. Holm.—p. 599.

Percutaneous Tuberculin Plaster Test.—Grut found that 82 per cent of 270 adults with a positive Mantoux reaction gave a positive plaster reaction the first time and 12 per cent the second time, and that the reaction failed in a maximum of 6 per cent and a minimum of 1 per cent. He considers Monrad's plaster reaction a simple and reliable method which should replace Pirquet's reaction in children as well as in adults.